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TOTAL PANCREATECTOMY*

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FRAMINGHAM, MASSACHUSETTS

AN INCREASING interest in surgery of the pancreas has been manifested since the demonstration by Whipple,[1] in 1935, of the practicability of partial pancreatectomy for the relief of cancer arising in or about the head of the pancreas. A natural outgrowth of this interest is recent efforts aimed at the feasibility of total pancreatectomy not only for the elimination of more extensive cancers but also for the relief of certain types of benign pancreatic disease. To date 16 cases of total pancreatectomy have been reported in the literature. Because the physiologic changes incident to total pancreatectomy in man are as yet imperfectly understood, it is important that observations made during and subsequent to this type of surgery be reported, so that the accumulated experience may eventually permit evaluation of its proper place in treatment. The purpose of this communication is to review the pertinent literature and to present a case of carcinoma involving the entire pancreas recently treated at the Framingham Union Hospital. In addition to resection of all of the pancreas the following structures were removed at operation: the spleen, the pyloric antrum of the stomach, all of the duodenum, 15 cm. of jejunum, the lower half of the common bile duct and the right half of the transverse colon.

CASE REPORT

A 70-year-old man was admitted to the hospital on May 23, 1947, complaining of upper abdominal pain of 4 months' duration. Two years before admission the patient had begun to limit his diet, without medical advice, because of obesity. This was followed by gradual loss of weight, which had become somewhat accelerated during the last 4 months and which totaled 32 pounds. One year before admission the gradual onset of constipation was noted. This became gradually worse and, during the last 6 months, required a daily enema. Occasional tarry stools had been noted, but there had been no gross blood. Four months before admission he applied strong pressure to the lower sternal and epigastric regions in using a heavy electric drill, which "shook him up" considerably. Four hours later he noted the sudden onset of epigastric pain, which since then had been more or less constantly present and which was described as a gnawing sensation radiating to the midline of the lower dorsal region. The pain was aggravated by food, was partially relieved by sitting or standing and by pressure applied to the epigastrium, and was not affected by alkalis. One month before admission an x-ray diagnosis of duodenal ulcer was made at another institution, and the patient was placed on a six-meal bland diet without relief. Two weeks before admission increasing pallor and weakness associated with some dyspnea on exertion was noted. At about that time he also noted slight itching of the skin. The urine was dark, although the stools were normal in color or occasionally tarry black. On the day of admission, while driving his car, he suddenly became euphoric and somewhat disoriented. This condition persisted for about 2 hours, after which his mental state gradually returned to normal. The patient was known to have had hypertension for about 6 months, but when he was seen by a physician after this episode, the blood pressure was found to be 125/70.

A review of the systems indicated no symptoms except nocturia of several years' duration. The past and family histories were noncontributory.

Physical examination revealed an elderly, thin, pale man in no distress. There was a slight icteric tint to the skin and scleras. The head, neck and chest were normal. The heart was not enlarged, rhythm was regular, and there were no murmurs. The lungs were clear. The abdomen was soft and readily examined. There was slight tenderness in the midline between the xiphoid and umbilicus but no muscle spasm or rebound tenderness. No masses were palpable. The genitalia and extremities were normal; the prostate was not palpably enlarged, and no masses were felt by rectum.

The temperature, pulse and respirations were normal. The blood pressure was 140/70.

The specific gravity of the urine varied from 1.003 to 1.016. Bile was present in each of seven specimens, but there was no albumin or sugar. Except for an occasional white cell the sediment was normal. No urobilinogen was found in either of two specimens tested. Examination of the blood disclosed a red-cell count of 2,050,000, with a hemoglobin of 6.5 gm. per 100 cc., and a white-cell count of 5600. The blood smear was normal except for moderate hypochromia. The blood sugar was 141 mg. per 100 cc. on the day after admission and 95 mg. several days later. The nonprotein nitrogen was 56 mg. per 100 cc. on admission, falling to 37 mg. on the day before operation. The total protein was reported as 6.0 gm. per 100 cc., with an albumin-globulin ratio of 4.4:1. After the transfusion of 4500 cc. of blood over the following 12 days, the total protein was 8.0 gm. per 100 cc., with an albumin-globulin ratio of 1:1. The prothrombin time was within normal limits, and the initial icteric index was 16. Two attempts to determine the total blood volume by the use of the dye T-1824 were frustrated by the presence of jaundice, which made it impossible to obtain satisfactory colorimetric readings. The presence of the blue dye in the blood serum made it impossible to secure satisfactory readings of the icteric index subsequent to admission, although clinically the patient became progressively more jaundiced. Each of nine stool specimens was strongly positive for occult blood, and one was reported to be negative. The stools were brown during the early part

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of the hospital stay but became clay colored thereafter. Gastric analysis revealed no free hydrochloric acid.

Electrocardiographic tracings disclosed left-axis deviation but were otherwise normal. X-ray examination of the chest showed the lungs to be clear; the heart was not enlarged. A barium enema demonstrated that the colon was normal. The esophagus and stomach were normal on gastrointestinal x-ray study. There was definite widening of the duodenal loop, indicating enlargement of the head of the pancreas. The duodenal mucosa revealed no evidence of ulceration; a cholecystogram was not done because of the presence of jaundice.

The patient was studied for 12 days preceding operation, during which the temperature, pulse and respirations were within normal limits. The blood pressure gradually rose from 140/70 on admission to 200/90 on the day before operation. The icterus became progressively deeper; the urine continued to show the presence of bile, and the stools changed from brown to clay colored. Food and fluids were well tolerated, and the diet was supplemented by daily intramuscular injections of crude liver extract, vitamin C and vitamin K. The prothrombin time did not vary significantly from the normal. Although the patient had Type A, Rh− blood, a total of 4500 cc. of whole blood was given without reaction, and at the end of the preoperative period he was considered to be a fair operative risk.

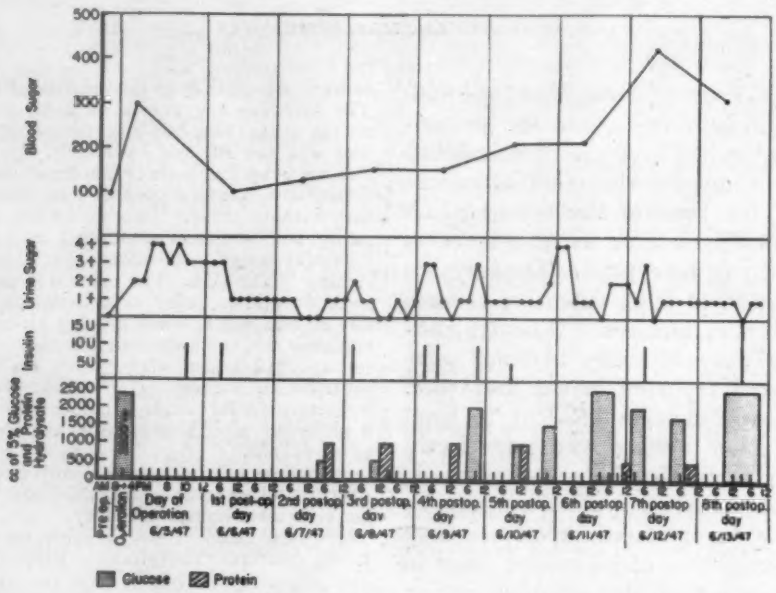

FIGURE 1. *The Diabetic State after Total Pancreatectomy.*

Operation was performed June 5 under continuous spinal anesthesia supplemented with intravenous Pentothal Sodium and small amounts of ether. A long, right-rectus-muscle-splitting incision was made and later enlarged by a connecting transverse incision extending across the upper abdomen to the left costal margin. The entire head, neck, body and tail of the pancreas were indurated, apparently owing to diffuse invasion by a neoplastic process that had not grossly invaded the surrounding structures. The liver was dark from jaundice and slightly enlarged but contained no metastatic nodules. The gall bladder was thin walled and markedly distended with thick, black bile, which was aspirated to facilitate exposure. The common bile duct was about 1.5 cm. in diameter. After the gastrocolic omentum had been divided a biopsy of the middle of the body of the pancreas was submitted to Dr. C. G. Tedeschi for frozen-section examination and was reported as showing the presence of carcinoma. Since the entire pancreas was obviously involved a total pancreatectomy was decided upon.

The stomach was divided about 7.5 cm. proximal to the pyloric sphincter, and the duodenum mobilized. The gastroduodenal vessels were identified and divided. The common bile duct was freed from the portal vein and hepatic artery and divided in its supraduodenal portion; the portal vein was accidentally lacerated but was satisfactorily repaired. The neck of the pancreas was easily freed from the underlying portal and superior mesenteric veins. The uncinate process was small and not adherent to the superior mesenteric vessels and was easily dissected free. At this point it was found that the blood supply to the transverse colon was anomalous and that the vessels supplying the right half extended through the neoplastic mass in the head of the pancreas. After the duodenum had been divided at the ligament of Treitz and mobilized to the right under the superior mesenteric vessels, the anomalous vessels to the right half of the transverse colon were divided, completing the mobilization of the duodenum and the head of the pancreas. Exposure for the mobilization of the body and tail of the pancreas was then greatly facilitated by division of the pancreas at its neck and removal of the mobilized pyloric antrum, duodenum and head of the pancreas. It was then evident that the splenic vessels were surrounded by neoplastic tissue. The spleen was therefore mobilized by division of the short gastric and left gastroepiploic vessels. The splenic artery and vein were divided close to their points of origin, and the body and tail of the pancreas and the spleen were removed.

After about 15 cm. of jejunum distal to the ligament of Treitz had been resected to assure an adequate blood supply, the end of the jejunum was closed. A loop of proximal jejunum was brought through a rent in the transverse mesocolon, and end-to-side anastomoses were completed between the jejunum and the stumps of the stomach and common bile duct, the latter about 10 cm. distal to the former. After these had been completed it was evident that the blood supply to the right half of the transverse colon was inadequate. The hepatic flexure of the colon was mobilized, and the right half of the transverse colon delivered through the middle of the wound and amputated over clamps to form a double-barreled colostomy. A catheter was sutured into the gall bladder and brought out through a stab wound in the right flank. A rubber tissue drain was placed in the bed of the pancreas and brought out through a second stab wound in the right flank. The wound was closed around the two loops of the transverse colostomy.

During the operation, which required 6½ hours, the patient received 2300 cc. of 5 per cent glucose in distilled water, 1500 cc. of whole blood and 300 cc. of plasma. The anesthesia required 455 mg. of procaine, 52 mg. of pontocaine, 1.5 gm. of Pentothal Sodium and 28.3 gm. of ether. The patient

withstood the operative procedure remarkably well, but when the operation had been completed the pulse rate was 130, and the blood pressure 90/55.

The immediate postoperative response to continued intravenous therapy was very satisfactory, the pulse rate and blood pressure rapidly approximating preoperative levels. careful attention to the diabetic state, since the entire pancreas had been removed.

The first 4 days of the postoperative course were remarkably smooth. The temperature and pulse curves progressively fell toward normal; peristalsis returned on the fourth day, and the patient was mentally alert and physically active.

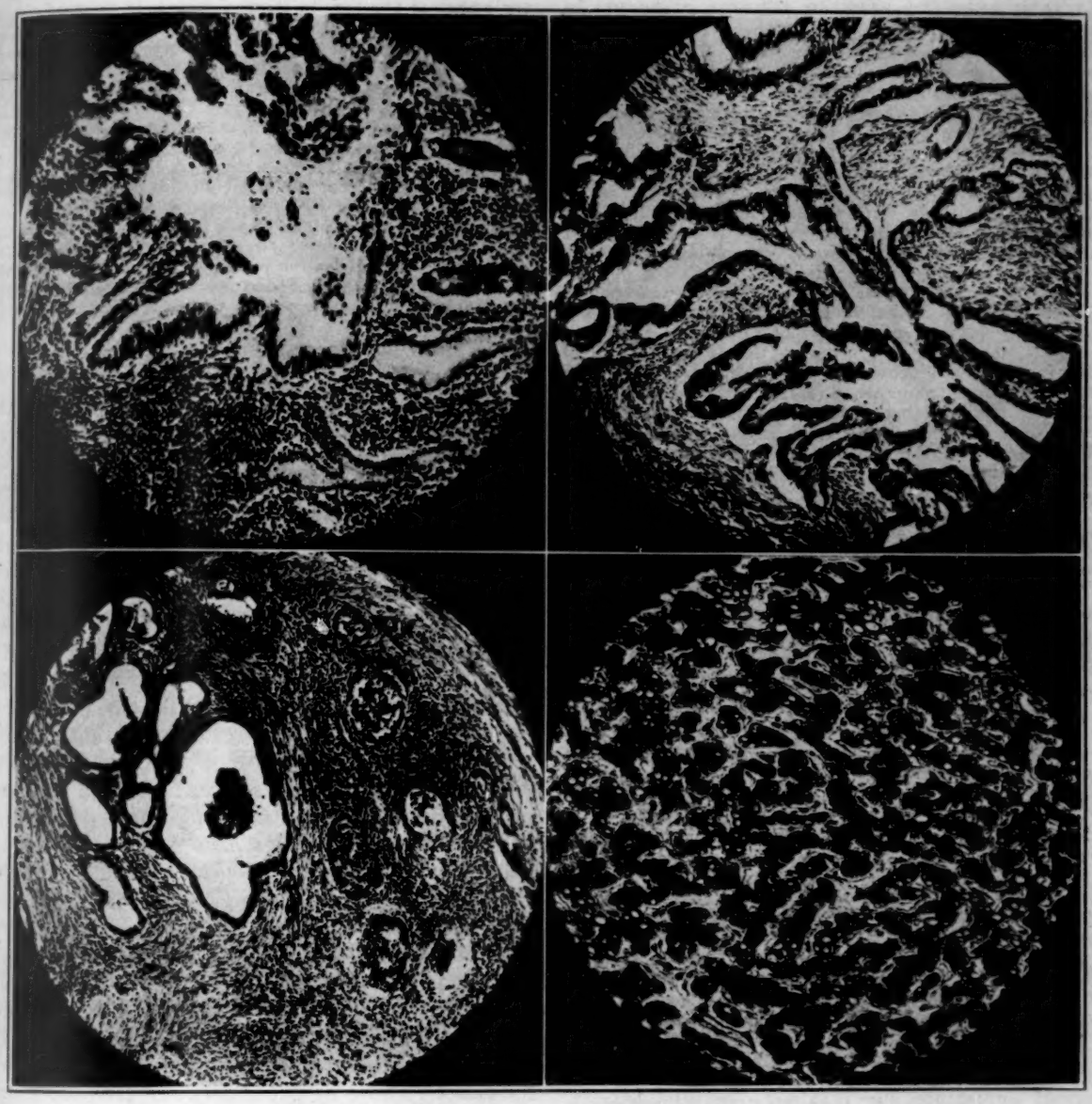

FIGURE 2.

A shows specimen from ulcerated area in second portion of duodenum, illustrating normal duodenal glands and closely adjacent adenocarcinoma. B demonstrates section from head of pancreas, showing extensive malignant infiltration. C illustrates portion from tail of pancreas, showing dilated ducts, one of which contains a clump of malignant cells (note enlargement of pancreatic islands). D demonstrates liver, showing some, but not marked, fatty replacement.

Postoperative treatment consisted in: decompression of the gastrointestinal tract by means of suction applied to a Levine tube, which was continued for 4 days; the administration of adequate intravenous fluids including glucose, physiologic saline solution, protein hydrolysate, plasma and whole blood (a total of 4000 cc. of blood during and after operation); penicillin and streptomycin in large doses; and

The proximal loop of the colostomy was opened at that time, and the wound appeared to be clean. On the evening of the 5th day the temperature rose to 101°F., and on the following day sepsis around the distal loop of the colostomy was discovered. The wound was opened, and extensive undermining by pus was discovered between the intact peritoneum and the overlying muscle. The entire septic area was widely

opened, cultured and packed with gauze, which was kept saturated with a mixture of urethane and penicillin.[2] At the same time the dose of penicillin, which until then had been 100,000 units every 3 hours, was increased to 500,000 units every 3 hours, to which 500 mg. of streptomycin was added. In spite of the most vigorous treatment the temperature and pulse continued to rise, and the patient became disoriented and finally comatose and died on the 8th postoperative day. The urinary output was maintained between 1200 and 2400 cc. daily, and yet the nonprotein nitrogen remained elevated to between 50 and 60 mg. per 100 cc. until the day before death, when it rose to 70, reaching 107 mg. per 100 cc. on the day of death. Throughout the postoperative course the serum chloride remained within normal limits, varying from 550 to 620 mg. per 100 cc. The cholecystostomy drained relatively small amounts of bile, the maximum being 320 cc. on the 2nd postoperative day. The icteric index fluctuated between 49 and 59 until the day of death, when it reached 75.

The postoperative diabetic state was followed closely. Fresh urine specimens were tested hourly for sugar and diacetic acid for 3 days and every 3 hours thereafter. The blood sugar level and carbon dioxide combining power were determined daily. At no time did the urine show diacetic acid, and the carbon dioxide combining power was consistently within normal limits, ranging from 53 to 69 vol. per cent. Figure 1 shows graphically the relation of the levels of sugar in the blood and urine to the administration of insulin, intravenous glucose and protein hydrolysate. As in other cases of total pancreatectomy, this patient proved to be relatively mildly diabetic. Because of the increased sensitivity to insulin reported after total pancreatectomy, efforts in the treatment of the diabetes were directed to the prevention of acidosis rather than to the maintenance of normal blood sugar levels.

It will be noted from Figure 1 that in spite of the administration of 115 gm. of intravenous glucose during operation only 20 units of insulin was given during the next 17 hours. At the end of that period the blood sugar level was 101 mg. per 100 cc. During the next 30 hours during which neither glucose nor insulin was administered, the urinary excretion of sugar fell to zero, and the blood sugar remained within normal limits. The largest amount of insulin required during any 24-hour period was during the 4th postoperative day, when a total of 30 units was given. From the 5th to the 8th postoperative day there was a progressive rise in blood sugar levels that was probably related not only to the increased administration of glucose and protein hydrolysate but also to the onset of sepsis.

Because of the short period of survival following the operation, there was no opportunity to make observations on the effects of elimination of other pancreatic secretions. However, on the 5th day after operation the serum lipase was reported as 0.1 cc. N/20 NaOH (normal, 0.1 to 1.0 cc.).

The surgical specimen consisted of the distal 6 cm. of stomach, all of the duodenum and an additional 10 cm. of upper jejunum, all of the pancreas and spleen and 24 cm. of transverse colon. The resected stomach and jejunum showed no gross or microscopical abnormalities. The transverse colon showed gross and microscopical evidence of infarction (due to ligation of its blood supply at operation) with widespread hemorrhagic changes and vascular congestion affecting all coats, the mucosa most severely. The entire head, body and tail of the pancreas were indurated and of variegated appearance due to alternating yellowish-pink, lobulated areas still preserving the characteristics of pancreatic tissue, and of grayish-pink, translucent areas suggesting neoplastic tissue. An area of indurated ulceration 2 cm. in diameter was found on the lesser curvature of the second portion of the duodenum. On microscopical examination this area of the duodenum, as well as the entire pancreas, showed evidence of a neoplastic process characterized by atypical glandular structures and by anaplastic cells disposed in cords or in rudimentary alveoli imbedded in fibrous connective tissue. The pancreatic islands were well preserved and, particularly in the region of the tail, appeared to be larger than normal (Fig. 2*A*, *B* and *C*). The spleen showed no gross or microscopical abnormalities.

Autopsy was performed 1¼ hours post mortem. About 200 cc. of purulent, blood-tinged fluid was found encysted between the lesser curvature of the stomach and the liver. From this fluid were cultured *Escherichia coli*, *Proteus vulgaris* and *Pseudomonas aeruginosa*. A second area of encysted fluid, containing about 600 cc., was observed in the bed of the removed spleen. This fluid was watery and blood tinged and was not infected. The remainder of the abdominal cavity was clean. The gastrojejunal and choledochojejunal anastomoses were well healed and patent.

The liver was somewhat enlarged, weighing 1500 gm., and except for moderate jaundice disclosed no gross abnormalities. On microscopical examination the liver cells in the center of the lobules showed regressive changes ranging from cloudy swelling to fatty degeneration, which, however, was moderate and did not compare with the extensive changes noted in a depancreatized dog (Fig. 2*D*). Bile casts were noted as well as a patchy distribution of inflammatory cells, chiefly lymphocytes and histiocytes. The Kupffer cells stood out conspicuously, and many were seen to contain blocks and granules of yellowish-brown pigment.

No gross evidence of metastasis was found. However, on microscopical examination small clumps of neoplastic cells similar to those found in the pancreas were found in both the cortex and the medulla of the left adrenal gland. Other important autopsy findings were generalized atherosclerosis, hypertrophy and dilatation of the left ventricle, myocardial fibrosis, left hydrothorax, pulmonary congestion and edema, purulent bronchitis and bronchiolitis and renal arteriosclerosis.

Surgical Results

The first authenticated case of total pancreatectomy was reported by Rockey[3] in 1943. This operation was performed for carcinoma arising in the body of the pancreas. The patient survived fifteen days, succumbing to bile peritonitis due to a "blow out" of the ligated end of the common bile duct. Of historical interest only are 2 cases culled from the literature by Sauve[4] in both of which nearly total pancreatectomies were done. The first of these was credited to Billroth by Mayo–Robson in 1901, the operation having been done in 1884. Since this case was never fully reported the exact extent of the operation and the end result are unknown. The second case was reported by Franke in 1900. This operation was also done for cancer of the pancreas, but the duodenum was not removed and a mass of pancreatic tissue "the size of a hazel nut" was left behind. Only transient glycosuria developed rather than severe diabetes as might have been expected from recent experimental findings discussed below. The patient survived five and a half months, dying from recurrent cancer.

The 16 reported cases of total pancreatectomy, together with the case presented above, are described in Table 1. Eleven operations were done for cancer, and only 3 patients survived the immediate postoperative period — an operative mortality of 73 per cent. Of the 3 who survived operation, 1 died in three and a half months of carcinomatosis, the second was living without known recurrence four months after operation, and the third was living with probable recurrence fifteen months after operation. It appears that the efficacy of total pancreatectomy for the cure of malignant tumors remains to be demonstrated. Of the 6 patients with benign disease, 4 were operated upon for pancreaticolithiasis, with an operative mortality of 50 per cent. Of the 2 survivors, 1 died of an in-

sulin reaction at the end of two and a half months, and the other was alive and free of abdominal pain a year after operation, but institutionalized because of pulmonary tuberculosis. Pancreatectomy was performed in the remaining 2 cases because of hyperinsulinism due to islet-cell adenomas that were small and so buried in the head of the pancreas that they could not be demonstrated at operation. At the time of the reports both patients were living and well, 1 thirty-seven months[6] and the other eight months[6] after operation. In the 17 cases of total pancreatectomy for all causes, 7 patients survived operation and 10 died, an operative mortality of 59 per cent.

Although, to date, the surgical mortality and the end results of total pancreatectomy leave much to be desired, it is probable that with increasing experience cure rates may be elevated and mortality figures reduced to acceptable limits. This has certainly been the experience with many operative procedures — for instance, with total gastrectomy — during recent years.

Physiologic Changes

The Diabetic State

The diabetic state that follows total pancreatectomy in man appears to be relatively mild. In the first case of total pancreatectomy, reported by Rockey,[3] the patient was given 67 units of insulin to cover intravenous glucose on the day of operation and 93 units on the following day. These doses were followed by severe and prolonged insulin reactions. Eventually, the daily insulin requirement was found to be only 27 units. Since then many authors have noted the relatively low insulin dosage required during the immediate postoperative period. To date only 7 patients have survived for longer periods, and these cases are listed in Table 2 along with the daily food intake and insulin requirement. In these cases the average daily insulin requirement was about 42 units, with a carbohydrate intake that averaged 289 gm.

Of particular interest in this connection are the cases reported by Brunschwig and his associates[10] and by Dixon et al.[19] In both these cases diabetes was present before total pancreatectomy was done. One patient, a fifty-three-year-old man, had had known diabetes for nine months preceding operation.[10] During the preoperative period, during which his weight was 72 kg. (158 lb.), the diabetes was controlled by 40 to 65 units of insulin per day on a diet of 398 gm. of carbohydrate, 200 gm. of protein and 12 gm. of fat (glucose equivalent of 511 gm.). Two months after operation the insulin requirement was reduced to about 40 units per day on a diet of 401 gm. of carbohydrate, 102 gm. of protein and 11 gm. of fat (glucose equivalent of 459 gm.). At that time the body weight had fallen to 56 kg. (123 lb.). The authors point out that the apparent reduction in the demand for insulin may have been due to two factors: the lower glucose value of the postoperative diet and the loss of 16 kg. of weight. The striking fact, however, is not that the insulin requirement was not more greatly reduced but that it was not greatly augmented by total pancreatectomy. From these observations the authors conclude that the insulin production of the normal pancreas is in the range of 30 to 50 units per day and that in diabetic patients requiring more than this amount, an extrainsular factor must be contributing to the diabetic syndrome.

The patient of Dixon et al.[19] was a fifty-year-old man who had known diabetes of nineteen months' duration before total pancreatectomy. During the preoperative period the diabetes was controlled with 24 units of protamine-zinc insulin daily. Seven months after operation 40 units of protamine-zinc insulin daily was required.

These and other observations have led to speculation regarding whether clinical diabetes, which often requires doses of insulin far in excess of those reported after total pancreatectomy, is entirely due to degeneration of insular tissue. Goldner and Clark,[9] after observations in 2 cases of total pancreatectomy with shorter survival periods, state that "The question must be raised whether in the causation of diabetes not only lack of insulin but also an insulin-inhibiting mechanism may play a role." Experimental evidence pointing in this direction was presented by Dragstedt, Allen and Smith,[20] who found the insulin requirement of partially depancreatized dogs to exceed that required after total pancreatectomy. Sprague,[6] however, believes that even if the insulin requirement of the depancreatized human being proves to be consistently less than that of many patients with severe diabetes, the conclusion that spontaneous diabetes and surgical diabetes are basically different is not justified. He points out that the insulin requirement in spontaneous diabetes is subject to a wide variety of influences, one of the most important of which is cachexia from any cause, which not only reduces the requirement for insulin but also may even lead to hypoglycemic coma without the administration of insulin. The poor nutritional state of patients after total pancreatectomy may well tend to ameliorate the diabetes and lower the insulin requirement. Furthermore, nothing is known of the effect of total pancreatectomy on the glycogenic and glycolytic functions of the liver, alterations of which might profoundly affect the diabetic state.

A state of apparently increased sensitivity to insulin has been present during the early postoperative period in nearly all reported cases, and Clagett's[17] patient died of an insulin reaction two and a half months after operation. These observations are of great importance in the management of patients after total pancreatectomy. It is evident that treatment during this period should be directed more toward the prevention of ketosis than to the control of the blood sugar levels. To date no case of

insulin resistance has been reported after total pancreatectomy.

Evidence that ketogenesis follows total pancreatectomy in man is scanty but indicates a similarity to that produced in untreated spontaneous diabetes and in depancreatized dogs. The patient of Brunschwig[10, 11] developed recurrent cancer, and three and a half months after operation, insulin was withdrawn. Glycosuria and ketosis promptly appeared, and death occurred in typical diabetic coma six days later. Dixon's[6] case was studied during two periods of insulin deprivation of eighty-nine hours each, the first beginning on the sixty-sixth and the second on the two hundred and forty-fifth postoperative day. During the first interval the diet contained 440 gm. of carbohydrate daily, and

TABLE 1. *Cases of Total Pancreatectomy Reported in the Literature.*

Case No.	Author	Sex	Age	Diagnosis	Other Operative Procedures	Survival	Cause of Death
			yr.				
1	Rockey[9]	M	51	Adenocarcinoma arising in body of pancreas	Partial (distal half) gastrectomy; total duodenectomy.	15 days	Bile peritonitis due to "blow out" of ligated common bile duct
2	Priestly et al.[5] Waugh et al.[6]	F	49	Hyperinsulinism due to islet-cell adenoma	Partial (distal third) gastrectomy; partial (first and second portions) duodenectomy.	Patient living and well 37 mo. after operation	—
3	Brunschwig[7] (Case H. H. 302199)	M	67	Carcinoma of entire pancreas	Total duodenectomy; splenectomy.	3 days	Massive bilateral pulmonary consolidation
4	Brunschwig[7] (Case N. R. 309791)	M	29	Diffuse carcinoma of pancreas	Total duodenectomy; splenectomy.	9 days	Exhaustion
5	McClure[8] (Case of Fallis)	M	46	Primary carcinoma of pancreas	Total duodenectomy; splenectomy.	Patient living and well 4 mo. after operation	—
6	Goldner and Clark[9] (Case of Brunschwig)	Not stated	Not stated	Carcinoma of bile duct invading pancreas	Not stated	11 days	Gastric hemorrhage; early peritonitis.
7	Goldner and Clark[9] (Case of Clark)	M	45	Papillary carcinoma of common bile duct with invasion into head of pancreas; chronic pancreatitis.	Partial duodenectomy; pylorectomy; splenectomy.	10 days	Hepatorenal failure and uremia
8	Brunschwig et al.[10] Ricketts et al.[11] Ricketts et al.[12] (Case F. W. 328218)	M	53	Carcinoma arising in body of pancreas with extension to stomach and left adrenal gland; metastasis to lymph nodes.	Total gastrectomy; total duodenectomy; splenectomy; left adrenalectomy; omentumectomy.	3½ mo.	Carcinomatosis and diabetic coma due to insulin withdrawal
9	Whipple[13]	F	26	Chronic pancreatitis; pancreaticolithiasis.	Pylorectomy; total duodenectomy.	Patient alive, with pulmonary tuberculosis, 1 yr. after operation	—
10	Whipple[13]	F	46	Fibrosis of pancreas; pancreaticolithiasis.	Pylorectomy; total duodenectomy; splenectomy.	7 days	Shock and pulmonary edema
11	Zinninger[14]	M	39	Chronic pancreatitis; pancreaticolithiasis.	Not stated	30 hr.	Not stated
12	Brunschwig[15]	Not stated	Not stated	Carcinoma of pancreas	Not stated	14 days	Not stated
13	Waugh et al.[6]	F	36	Hyperinsulinism due to islet-cell adenoma	Pylorectomy; partial duodenectomy.	Patient living and well 8 mo. after operation	—
14	Dixon[16]	M	50	Carcinoma arising in head and involving half of pancreas; remainder atrophic.	Partial gastrectomy (distal half); total duodenectomy; splenectomy.	Patient living with recurrent cancer 14 mo. after operation	—
15	Clagett[17]	F	37	Chronic pancreatitis; diffuse calcification of pancreas; multiple pancreatic calculi.	Partial gastrectomy; partial duodenectomy; splenectomy.	2½ mo.	Insulin reaction
16	Brunschwig[18] (Case 348369)	Not stated	Not stated	Sarcoma — origin not stated	Subtotal (seven eighths) gastrectomy; total duodenectomy; splenectomy; transverse colectomy.	19 days	Peritonitis due to leakage of gastrojejunal anastomosis
17	Gaston	M	70	Adenocarcinoma probably arising in papilla of Vater and invading entire pancreas	Pylorectomy; total duodenectomy; splenectomy; transverse colectomy.	8 days	Peritonitis secondary to wound sepsis; uremia.

whereas the blood sugar level rose to 813 mg. per 100 cc., the carbon dioxide combining power remained within normal limits and the urine showed a faint trace of acetone only during the last eight hours. During this interval the plasma chloride level fell to 507 mg. per 100 cc., and the patient complained of abdominal cramps, which were relieved by the administration of 3 gm. of sodium chloride by mouth. In spite of a large urinary output the blood urea rose to 57 mg. per 100 cc. During the second interval of insulin privation the diet contained only 120 gm. of carbohydrate, and a salt mixture was given to prevent the unpleasant symptoms associated with hypochloremia. On the lower carbohydrate intake liver glycogen was depleted, and conditions more favorable to the development

TABLE 1 (*Continued*).

CASE No.	DIET	DAILY INSULIN	EXTERNAL PANCREATIC SECRETION STUDIES	PLASMA LIPOIDS	LIVER AND LIVER-FUNCTION STUDIES	REMARKS
1	—	27 units; frequent insulin shock in early post-operative period.	—	—	Liver normal at autopsy	Slightly less than 1 gm. of pancreatic tissue found at autopsy
	Carbohydrate, 243 gm.; protein, 94 gm.; fat, 70 gm.	30 units	Recovered in feces: 35–70 per cent of ingested fat, 25–55 per cent of ingested nitrogen; recovered in urine and feces: 21–34 per cent of ingested calories.	Normal 37 mo. after operation	Bromsulfalein retention normal 30 mo. after operation	—
3	—	—	—	—	—	—
4	—	"Less than anticipated"	—	—	—	—
	—	26 units of protamine-zinc insulin daily; 8 units of regular insulin twice weekly.	—	—	—	—
6	150 to 200 gm. of glucose parenterally	50 units	—	—	—	—
7	150 to 200 gm. of glucose parenterally	30 to 40 units	—	—	—	Neoplasm extended into wall of portal vein and around celiac axis preventing complete eradication
8	Carbohydrate, 401 gm.; protein, 102 gm.; fat, 11 gm.	30 units of protamine-zinc insulin; 10 units of regular insulin (frequent hypoglycemic reactions).	—	Slowly declined but never abnormal	Liver fatty at autopsy, probably owing to death in diabetic coma	Patient diabetic before operation, requiring more insulin than after operation; preoperative diabetes spontaneous and not due to tumor.
9	Carbohydrate, 300 gm.; protein, 70 gm.; fat, 75 gm.	30 to 80 units	—	—	—	—
10	—	50 to 90 units (failed to control glycosuria)	—	—	—	Autopsy revealed localized bile peritonitis and thrombosis of large branch of portal vein
11	—	30 to 50 units	—	—	—	—
12	—	Not stated	—	—	—	—
13	Carbohydrate, 267 gm.; protein, 125 gm.; fat, 103 gm.	26 units of regular insulin; 6 units of protamine-zinc insulin.	—	Normal 70 days postoperatively; slightly below normal 123 days postoperatively; probably due to jaundice.	—	—
14	Carbohydrate, 272 gm.; protein, 107 gm.; fat, 100 gm.	30 units of regular insulin; 10 units of protamine-zinc insulin.	Nitrogen loss in stools, 4 to 8 gm. (normal, less than 1.5 gm.); fat loss in stools, 36 to 48 gm. (normal, 6 to 7 gm.).	Increase of 100 per cent 8 mo. after operation	Bromsulfalein retention normal 8 mo. after operation	Patient diabetic 19 mo. before operation, requiring 20 units of insulin daily
15	Carbohydrate, 250 gm.; protein, 75 gm.; fat, 101 gm.	30 units of regular insulin; 8 units of protamine-zinc insulin.	—	Normal 1 mo. after operation	Bromsulfalein retention normal 1 mo. after operation	Prolonged drainage of common bile duct did not relieve symptoms before pancreatectomy
16	—	"Diabetes did not appear unusually severe or difficult to control"	—	—	—	—
17	50 to 150 gm. of glucose daily parenterally	10 to 30 units regular insulin daily	—	—	Liver normal at autopsy	—

of ketosis were provided. During the second period ketonemia was marked.

At this time no information is available regarding whether totally depancreatized human beings will eventually develop the degenerative changes associated with prolonged spontaneous diabetes, although atheromatosis and arteriosclerosis have been reported in depancreatized dogs.[21]

Liver Changes

It has long been known that totally depancreatized dogs maintained on adequate diets and insulin cannot be kept in a state of health for long periods. After four to six weeks on such a regime the animals begin to show a decrease in glucose excretion, increased insulin sensitivity, hypolipemia and a loss of appetite with cachexia. The general condition progressively deteriorates and ends in death, usually within a few months. At autopsy a majority of the animals, but not all, display a remarkable accumulation of fat in the liver, and the resulting impairment of liver function can be accurately estimated before death by the degree of retention of bromsulfalein.[22] Fisher[23] and Allan et al.[24] showed in 1924 that the addition of raw pancreas to the diet effectively prevented the changes in the liver and that the animals could be maintained in a state of health for long periods. Lecithin[25, 26] and later choline[27, 28] were found to prevent the deposition of fat in the liver when added to the diet in adequate quantities and also to cause the liver to return to normal after the condition had developed. More recently methionine has been shown to possess the same properties of prevention and cure.[6, 29]

In addition to the substances listed above, Dragstedt[21, 30, 31] has identified what he believes to be a second internal secretion of the pancreas, probably formed in the alpha cells, which has remarkable properties for preventing or curing the liver changes resulting from total pancreatectomy in dogs. This substance, which he terms "Lipocaic," is not present in the external secretion of the pancreas and has been prepared free of lecithin and practically free of choline. Since it has been found only in extracts of pancreas and not in extracts of other organs rich in lecithin, it probably represents a true internal secretion of the pancreas.

Associated with the fatty changes in the liver is a gradual reduction in plasma lipoids that begins four or five weeks after pancreatectomy in dogs and falls to about 50 per cent of the normal level by the twentieth week after operation.[32]

Few observations are available concerning the plasma lipoids and liver function in totally depancreatized human beings. Plasma lipoid studies have been reported in 5 of the 17 cases in the literature (Cases 2, 8, 13, 14 and 15 in Table 1). Of the cases in Table 1, Cases 2 and 15 showed normal plasma lipoids thirty-seven months and one month, respectively, after operation. In Case 8 the values of plasma lipoids slowly declined during the three and a half months of survival but were never abnormal. In Case 13 the plasma lipoids were normal seventy days after operation but were slightly below normal on the hundred and twenty-third day. At the later examination the patient was jaundiced, and this fact may have played a part in lowering the values. In Case 14 a 100 per cent increase in plasma lipoids was found eight months after operation. The explanation of this is not clear, since at the same time the bromsulfalein retention was normal and exactly the opposite occurs after pancreatectomy in dogs.

The condition of the liver at autopsy has been described in 3 cases (Cases 1, 8 and 17 in Table 1). In 2 of these it was found to be normal fifteen days and eight days, respectively, after operation. In the other case the liver was described as fatty three and a half months after operation, but the cause of death was diabetic coma due to insulin withdrawal, which may have been responsible for the findings.

Bromsulfalein liver-function studies have been reported in 3 cases (Cases 2, 14 and 15 in Table 1) and were normal in all thirty-seven months, eight months and one month, respectively, after operation.

Although material concerning the effects of total pancreatectomy on the liver in man is scanty, it is evident from the discussion presented above that the gross fatty changes noted in depancreatized dogs have not been observed either clinically or at

TABLE 2. *Insulin Requirement in Patients Surviving Immediate Postoperative Period.*

Author	Age of Patient	Sex	Time of Survival	Daily Food Intake			Daily Insulin Requirement
				carbohydrate	protein	fat	
	yr.		mo.	gm.	gm.	gm.	units
Priestly et al.[5]	49	F	37	243	94	70	30
McClure[8]	46	M	4				26–34
Brunschwig[7]	53	M	3½	401	102	11	40
Whipple[15]	26	F	12	300	70	75	30–80
Waugh et al.[6]	36	F	8	267	125	103	32
Dixon[19]	50	M	14	272	107	100	40
Clagett[17]	37	F	2½	250	75	101	38

autopsy. However, changes similar to those seen in the dog and responding to the administration of lipocaic have been observed in spontaneous diabetes[33] and after destruction of the pancreas from repeated attacks of acute pancreatitis.[30] From these observations it is unlikely that the failure to observe in man the liver changes noted in the dog is due to a species immunity, although this factor must be considered, since it is well known that there is great variation in the severity of the diabetes and in the ability to form ketone bodies among different species of animals after depancreatization. It is more probable that the presence of choline and other lipotrophic substances in the diet of man is sufficient to protect the liver.

Digestion and Absorption

Experiences after ligation of the pancreatic ducts incident to partial pancreatectomy have led to conflicting reports on the effects of exclusion of the external secretion of the pancreas from the gastrointestinal tract.[34–36] Some patients develop bulky, frothy, foul-smelling stools, which contain large percentages of the ingested fat and nitrogen, whereas others remain relatively unaffected. Similar though less extensive loss of fat and nitrogen has been demonstrated after partial gastrectomy done for the relief of duodenal ulcer.[37, 38] Experimental work on dogs after complete pancreatectomy, the production of a complete pancreatic fistula or evulsion of the pancreatic ducts showed a marked loss of fat and carbohydrate in the feces.[39, 40] An increased excretion of fecal nitrogen was related to the increased bulk of the feces, which was less when diets rich in protein were employed. After evulsion of the pancreatic ducts there was a gradual failure of utilization of food, whereas the failure promptly followed total pancreatectomy or complete pancreatic fistula, leading to the conjecture that enzymes sufficient for the normal utilization of foodstuffs are absorbed from the obstructed pancreatic ducts. These experimental findings may explain the antithetical results noted in human patients after partial pancreatectomy.

Careful metabolic studies have been reported in only 2 cases of total pancreatectomy in man.[5, 6, 19] In these cases the stools were bulky, light, soft and usually formed. The average daily weight of the stool was two or three times that of normal subjects, largely owing to the excretion of large amounts of fat and protein. The average daily amount of fat eliminated in the stools was five to seven times the amount eliminated by normal persons, and the daily elimination of nitrogen was two and a half to seven times the normal amount.

Of the large amount of fat recovered in the stools, approximately a third was recovered as neutral fat, and the remainder as fatty acid, indicating that, in spite of the total absence of pancreatic enzymes, the splitting of fat was highly successful. The administration of pancreatin, a commercial extract of pancreas, in doses of 15 gm. per day caused an appreciable reduction in the loss of fat and nitrogen in the feces and a corresponding lowering of the bulk of the stools. On pancreatin therapy, however, there was no significant change in the percentage of nitrogen and fat in the stools, nor was there any change in the percentage of fat recovered as neutral fat and fatty acid. The administration of pancreatin was found to be highly useful in reducing the loss of calories in the stool. In one case 23.9 per cent of the ingested calories were lost in the stool during a test period on a carefully weighed diet.[10] During a second test period on the same diet, but with the addition of pancreatin, the caloric loss was reduced to 12.5 per cent. Although the nitrogen balance of this patient was positive even in the absence of pancreatin, the use of this drug made the maintenance of a positive nitrogen balance much easier.

Discussion

In the present state of knowledge of the physiologic effects of total pancreatectomy in man the following points regarding the postoperative treatment of such cases may be emphasized.

The diabetes that follows total pancreatectomy is relatively mild and, at least in the early postoperative period, appears to be associated with an increased insulin sensitivity. Because of this, hypoglycemic reactions, which may be severe or even fatal, should be carefully avoided. Early treatment of the diabetic state should be directed toward the prevention of ketosis rather than to the rigid control of blood sugar levels.

The fatty liver associated with total pancreatectomy in dogs has not been observed in man, but this is probably not a species immunity. Prevention of this disorder can probably be effected by a diet rich in choline. About 2 gm. of choline daily is required to prevent fatty liver in pancreatectomized dogs. One egg yolk contains about 0.5 gm. of choline, and liver and other glandular meats contain large amounts. In addition, choline chloride and methionine are available commercially and may be used to supplement the diet. In patients who survive for long periods, an occasional check on the level of plasma lipoids, as well as on the size of the liver as noted clinically, should give warning that fatty metamorphosis is taking place.

Because of the poor fat digestion in the total absence of pancreatic secretion, the stools tend to be bulky and frequent, and these changes are more marked the higher the fat content of the diet. For these reasons the postoperative diet should be low in fat, the caloric intake being made up with carbohydrates, which are well tolerated. In addition, pancreatin, in doses of 15 gm. daily, should be administered to increase the absorption of fat and protein and to aid in the maintenance of nitrogen equilibrium.

Summary

A case of diffuse carcinoma of the pancreas treated by total pancreatectomy is presented, together with an analysis of similar cases reported in the literature.

The surgical mortality of total pancreatectomy is high, and the conditions demanding this type of procedure are not commonly encountered. With increasing experience the surgical mortality can probably be reduced to acceptable limits.

The physiologic changes that follow total pancreatectomy are discussed from the standpoint of the diabetic state, the liver changes and the loss of the external pancreatic secretions.

Suggestions for the postoperative care of patients after total pancreatectomy are presented.

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PULMONARY TULAREMIA IN MASSACHUSETTS

Report of a Case Due to Tick Bites

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TULAREMIA is a relatively rare disease in New England. The pulmonary form, which is even less common, occurs in Massachusetts, as in the case reported below. It is important to recognize the presence of *Pasteurella tularensis* and its many reservoirs and transmitting agents, for a specific treatment is now available in streptomycin. Otherwise, the pulmonary form is fatal in 40 to 50 per cent of cases. Because of this fact a case of the pulmonary form occurring in a resident of Cape Cod who showed excellent response to streptomycin therapy is reported below.

Tularemia has been reported in every New England state except Vermont.[1] Contact with *Past. tularensis* has been noted through the following animals: rabbits, ground squirrels, cats, grouse, mink, sheep, swine and skunk.[2] The great reservoir of infection and the greatest source of human infection is the wild rabbit (jack, cotton tail and snowshoe varieties), but owing to the agency of blood-sucking insects common to rabbits and man, cases also result from tick bites and fly bites.[3] The disease should be suspected more strongly in the months from March to October, the period of greatest tick activity. The disease is transmitted and maintained in animals by *Dermacentor andersoni* (the wood tick), *Chrysops discalis* (the horsefly), *Haemaphysalis leporis-palustris* (the rabbit tick) and *Dermacentor variabilis* (the American dog tick).[4, 5] The fact that this disease may result from the bites of ticks or flies or from contamination of the skin or conjunctiva with the tissues or body fluids of infected rodents, flies or ticks is not fully appreciated.

CASE REPORT

A 68-year-old retired physician, a resident of Duxbury, Massachusetts, was admitted to the hospital on June 9, 1947, because of fever of about 6 days' duration. The patient's residence was important in that he lived on Cape Cod in an area where ticks were especially plentiful in that year. The patient spent much of his time in the woods and fields and for the past month had noted frequent tick bites about his legs. The patient's dog, with which he was in frequent contact, was often infested with ticks, and the patient removed and crushed 10 to 15 ticks daily from the animal. About a week before admission the dog was said to have killed and eaten a rabbit after which the dog seemed "sickly" for several days. About 4 years previously a neighbor had been hospitalized for an "infected tick bite" and had noted fever and headache for approximately 2 weeks. In the week before admission, the patient incurred a number of tick bites on his left leg and picked off a number of ticks each night. The illness began about 6 days before entry, with the onset of moderate anorexia and a stabbing pain in the left parietal region. These symptoms increased in intensity for the next few days with the addition of gradually rising temperature to 104°F. Mild, shaking chills were noted on the 3rd day of the illness. On the day before admission the temperature remained persistently elevated to 103 to 104°F., and the patient showed much mental confusion. There had been no pulmonary symptoms, abdominal pain or change in bowel habits.

Physical examination revealed a well developed, well nourished, elderly man who was markedly confused, lethargic and irritable. There were multiple small (2 or 3 mm.) scabby lesions over the lateral area of the left leg, said to be tick bites; none were ulcerous or appeared infected. The tongue was mildly thickened and covered with a grayish coat. There were no palpable lymph nodes in any area of the body. Examination of the chest disclosed no abnormalities. Neurologic examination was negative. The liver or spleen could not be palpated, but liver dullness extended about two fingerbreadths below the right costal margin.

Examination of the blood revealed a white-cell count of 10,500, with 94 per cent neutrophils. The nonprotein nitrogen was 46 mg. per 100 cc. The agglutination test for undulant fever, the Weil–Felix reaction and agglutinations for *Proteus vulgaris* (strains XK, X19 and X2) were negative. Agglutinations for *Eberthella typhosa*, *Salmonella paratyphi* (B), *S. choleraesuis* and *Shigella paradysenteriae* (Sonne and Flexner) were also negative. The heterophil-antibody test was within normal limits, and the test for cold agglutinins was negative. Serum sent to the United States Public Health Service for agglutination for *Past. tularensis* was reported as negative.

The temperature remained at about 104°F., and the pulse remained above 100 for the first 24 hours. The patient was nauseated and vomited several times. He complained of severe frontal headache and was apathetic and mentally confused, but he demonstrated no additional physical signs. Lumbar puncture showed the cerebrospinal fluid to be within normal limits. On the following day the temperature ranged between 102 and 104°F., and the pulse between 90 and 100. The patient still exhibited no pulmonary symptoms, but physical examination revealed dullness to percussion, decreased breath sounds and a few coarse crackling rales over the left base, posteriorly. X-ray examination on the following day showed an area of more or less homogeneous increased density in the left lower-lung field. There was slight infiltration at both hili. The appearance was that of pneumonia. The patient was started on penicillin therapy, with no beneficial effects and with a temperature consistently elevated to 103 to 104°F., and became more lethargic, apathetic and mentally confused. A repeated cerebrospinal-fluid examination was within normal limits. Streptomycin therapy in a dosage of 0.25 gm. intramuscularly every 3 hours was instituted on June 12, and after the patient had received 2 gm. for about 24 hours the temperature and pulse began to fall. The temperature reached normal on June 14 after the patient had received about 4.25 gm. of streptomycin. There was striking improvement of the symptoms of restlessness, irritability and mental confusion, and the patient stated that the severe headache had gone. The white-cell count decreased by 1000 daily for 5 days, but the differential count consistently showed over 90 per cent of the neutrophil series. Numerous blood cultures demonstrated no growths. Except for a rise in temperature to about 100°F. on June 14 and 15 the course of the disease was uneventful, and the temperature and pulse were within normal limits from June 14 to discharge on June 28. The patient had no recollection of the mental confusion and irritability.

The clinical course is demonstrated in Figure 1.

Serum sent to the United States Public Health Service on June 19 was reported as showing agglutination for *Past. tularensis* through a dilution of 1:640; agglutination for *Brucella abortus* through a dilution of 1:10; and agglutination

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for *Proteus vulgaris* (strain X19) through a dilution of 1:20. This substantiated the diagnosis of tularemia of the typhoidal type.

The pneumonia began to show signs of resolution on June 21, and the patient exhibited rapid improvement until discharge. He wished to continue convalescence at home and to be followed by his physician. X-ray study of the chest on June 25 demonstrated that consolidation was still present in the left lower lobe. There was slight radiolucency medially, suggesting beginning resolution.

Discussion

The public-health aspects presented by this case are important when it is realized that ticks represent a permanent reservoir of possible infection. The female can transmit the organism through the egg to the young, who then harbor them throughout their life.[6] Tularemia may simulate many diseases, such as meningitis, typhoid fever, Rocky Mountain spotted fever, atypical pneumonia, undulant fever and infectious mononucleosis. Owing to its variety it is frequently misdiagnosed as typhoid fever or pneumonia, so that it is essential to think of the disease in differential diagnosis. In Alberta, Canada, physicians include *Past. tularensis* as an antigen in routine agglutination tests for typhoid and related organisms, and by this means a small number of cases have been found that might have been missed.[2]

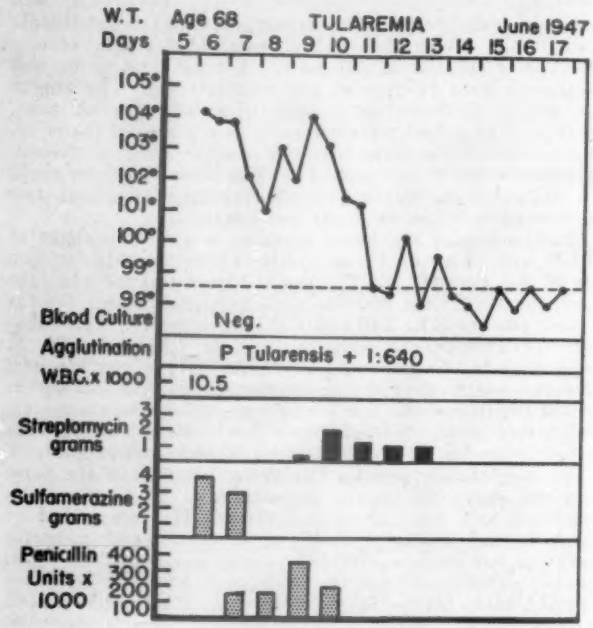

Figure 1.

Typhoidal tularemia comprises about 5 per cent of cases of tularemia, and both primary lesions and lymphadenitis are absent.[7] Instead, there is a general systemic infection in which fever and prostration are the outstanding symptoms. In the series studied by Warring and Ruffin[1] it was noted that delirium followed by drowsiness was most marked in the pulmonic type of the disease. In the more serious of these cases definite areas of consolidation involving one or several lobes appeared. Resolution of the pneumonia began in the third week and was very slow, requiring from five weeks to six months for completion. In a series reported by Francis[8] a bronchopneumonia type of lesion was the terminal condition in 5 cases, and a lobar-pneumonia type terminated fatally in 2 cases.

In fatal tularemia the most frequent pulmonary lesion is a pneumonia that is basically nodular or confluently nodular in character — sometimes lobar in extent — and involves one to all lobes.[8] The exudate is primarily monocytic and always shows more or less necrosis. In the central portions the septums are usually necrotic, with collagenous, reticular and elastic stroma persisting in considerable measure. Gram-positive cocci are often found in purulent exudates; usually copious delicately fibrillar, fibrinous exudates may be identified in some alveoli. The alveolar septums are congested in many cases, both in pneumonic areas and elsewhere. Serous exudation in the other congested areas is common. Vessels frequently show proliferative intimal reactions associated with mononuclear-cell infiltration and perhaps necrosis and thrombosis. The pleura shows fibrinous, fibrinocellular and fibrocaseous exudation in a number of cases.

Summary

A case of the pulmonary form of tularemia occurring in a resident of Massachusetts and successfully treated with streptomycin therapy is reported.

It is important to recognize the possibility of *Pasteurella tularensis* in the pulmonary form, for this disease is easily confused with others, and a specific treatment is now provided by streptomycin.

Owing to the agency of blood-sucking insects common to wild animals and to man, other cases may result from tick bites or fly bites. Ticks are reported to have shown a decided increase in 1947 in the Cape Cod region and have been noted north of Boston.

This was the first proved case of tularemia reported to the Massachusetts Department of Public Health for 1947. Seven cases in all were reported during 1947 — an unusually high incidence of the disease.

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PRESACRAL NEURECTOMY FOR DYSMENORRHEA*

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THIS paper deals with a series of presacral neurectomies performed for relief of dysmenorrhea. A total of 111 operations have been done at the Massachusetts General Hospital and the Palmer Memorial Hospital from 1930–1946. In most cases the neurectomy was combined with dilatation and curettage, a suspension and any other necessary pelvic surgery that the gynecologic situation demanded. These 111 cases can be divided into a group with essential dysmenorrhea and a group with acquired dysmenorrhea. The patients in the former group had severe crampy pain starting shortly after the menarche, with painful menstruation that severely upset their social and economic life; physical examination was negative. The patients with acquired dysmenorrhea had obvious pathologic processes to explain the painful periods. Table 1 gives the results in both groups.

TABLE 1. *Results of Presacral Neurectomy for Relief of Dysmenorrhea (1930–1946).*

RESULT*	PATIENTS WITH ESSENTIAL DYSMENORRHEA	PATIENTS WITH ACQUIRED DYSMENORRHEA
Complete relief	73 (81%)	10 (52.6%)
Partial relief	4 (4.5%)	4 (21%)
Failure	12 (14.5%)	5 (26.4%)
Totals	89	19

*There was no follow-up study in 3 cases.

Evaluation of results from the operation were based on a personal follow-up study in the majority of cases and by a follow-up letter in a few. There was little difference in early and late follow-up. If the operation was judged successful at six months the same report was received years later except in 2 cases, which are discussed below. The results were divided into patients with complete relief, those with equivocal or partial relief and those on whom the operation failed.

Complete relief was obtained in 81 per cent and partial relief in 4.5 per cent of patients with essential dysmenorrhea, and there were failures in 12, or 14.5 per cent. In contrast, in the group with acquired dysmenorrhea, in which there was an obvious cause for the pain, presacral neurectomy in addition to other gynecologic procedures gave complete relief in 52.6 per cent and partial relief in 21 per cent of cases, and in 26.4 per cent the operation failed; the causes of the dysmenorrhea in this group are presented in Table 2.

In this series there were no deaths. There were only 2 serious postoperative complications: severe small-bowel obstructions due to adhesions to the incision in the posterior peritoneum. Lysis of the adhesions was necessary after the intestinal obstruction had been relieved by Miller–Abbott tube. These complications of intestinal obstruction occurred in patients with acquired dysmenorrhea, both of whom had pelvic inflammatory disease.

TABLE 2. *Etiology in Patients with Acquired Dysmenorrhea.*

CAUSE	NO. OF CASES
Pelvic inflammation	4
Endometriosis	7
Post-partum dysmenorrhea	5
Post-appendectomy dysmenorrhea	3
Total	19

There was only 1 serious operative complication, a severe hemorrhage from the left common iliac vein when a small branch was avulsed. The rent in the vein was closed, arterial silk being used.

CAUSES OF FAILURE

Previous reports have adequately demonstrated the efficacy of presacral neurectomy in essential dysmenorrhea, which is now a standard operative procedure in pelvic surgery. However, Tucker[1] reports failures in 11 per cent of cases, Fontaine and Herman[2] in 13 per cent, and Meigs[3] in 15 per cent. Most authors have had about this same percentage of failures. And that is the group upon whom attention should be focused. Of course, the surgeon can calmly accept his 10 to 15 per cent failures and pay no attention to them, or label the patients psychoneurotics and send them to a psychiatrist after operation. In this study major interest was focused on the failures to determine if any measures could be taken to prevent failures in the future. Of great importance is the fact that the cause of dysmenorrhea is not actually known. Anatomic, functional and hormonal studies have not definitely proved what causes crampy pains with menstruation. Rational therapy without knowledge of the etiology is impossible. It is known that these patients are usually sensitive and emotional. Haman[4] has ac-

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curately shown that the pain sensitivity of the patient with dysmenorrhea is low, and the psychiatrists have long emphasized the role of the emotional background of women in this problem. It is our belief that all other means of curing dysmenorrhea should be tried before a presacral neurectomy is performed.

An analysis of the 12 cases in which presacral neurectomy failed to afford relief of essential dysmenorrhea showed that the three possible causes for the failure were psychoneurosis (3 cases), regeneration of the sympathetic nerves (2 cases) and incomplete sympathectomy (7 cases).

The first group comprises three cases judged to be psychoneurotic and emphasizes the importance of the careful choice of the patients. Care was taken in selecting these patients for presacral neurectomy, but the patients who were psychoneurotic, and possibly others in whom the operation failed, were nevertheless subjected to operation. The number of patients with dysmenorrhea who were not judged fit candidates for presacral neurectomy cannot be given, since there is no way in either ward or private practice to obtain the records of all patients with dysmenorrhea. Others have attempted to eliminate the psychoneurotic patients by various methods. Flothow[5] advocated a block of the second and third lumbar segments and also of the superior hypogastric plexus with 2 per cent procaine while the patient was experiencing dysmenorrhea; if relief of pain was produced, presacral neurectomy was advised. He cites an example of a patient with dysmenorrhea who was not relieved by his injection or by spinal anesthesia effective to the nipple line; she was not operated upon. Because of difficulty in obtaining hospital beds we have not used this injection method but have attempted to eliminate the psychoneurotic patients by another test.

TABLE 3. *Estrogen Test in Essential Dysmenorrhea.*

RESULT OF ESTROGEN WITHDRAWAL	SUCCESSFUL PRESACRAL NEURECTOMY	UNSUCCESSFUL PRESACRAL NEURECTOMY
	NO. OF CASES	NO. OF CASES
Painless bleeding	27	5
Painful bleeding	—	3

This test consists of preventing ovulation by the use of estrogen and then stopping the estrogen and allowing the patients to have withdrawal bleeding. Estrogen-withdrawal bleeding or anovulatory bleeding is painless in the normal, healthy female. A variety of estrogens have been used to stop ovulation. For example, diethylstilbestrol (1 mg. daily) may be given for twenty days, starting on the first day of menstruation; ovulation is prevented, and two to eight days after the stilbestrol is stopped withdrawal bleeding occurs and the patient has a painless period. If this test is carried out with inhibition of ovulation and the bleeding is still associated with pain, it is safe to assume that the patient has pain on experiencing any vaginal bleeding, and a psychiatrist rather than a surgeon should be consulted. This test is now carried out on all patients who have severe dysmenorrhea, and only those who have complete relief of pain after the estrogen withdrawal are operated upon.

Thirty-five patients were given estrogens and subsequently operated upon (Table 3). The significance of the test is illustrated by the patients who were not relieved of dysmenorrhea after the estrogens and on whom presacral neurectomy was nevertheless performed, resulting in failure. Two of these patients were seen by psychiatrists, and study showed them to be overly sensitive and their dysmenorrhea to be associated with intense emotional difficulties. The third patient had no relief preoperatively with estrogens, and operation was a failure. She too was sensitive, but it was difficult to prove any clean-cut psychoneurotic element in the dysmenorrhea. We believe that this test proves that if the estrogen-withdrawal bleeding is painful presacral neurectomy should not be done.

The second possible cause of failure of this operation is regeneration of the sympathetic nerves. Two cases in which presacral neurectomy failed may be accounted for on this basis. This problem of regeneration of the sympathetic nerves has plagued surgeons interested in other types of sympathectomy. This has been especially true in the dorsal sympathectomies for Raynaud's disease. The early operations done at the Massachusetts General Hospital successfully denervated the upper extremities, but within six months to a year the disease recurred. Sweating and skin-temperature tests showed that the sympathetic nerves had regenerated. Reoperation demonstrated the regenerated nerves. Smithwick[6] circumvented this regeneration in dorsal sympathectomies by attaching a silk cylinder around the cut nerve ends. In splanchnic resections for relief of abdominal pain regeneration also occurs, and relief by sympathectomy may be of short duration. Little mention has been made of this possibility after presacral neurectomy. Regeneration may account for 2 of the failures in our series. Both were considered successful cases with satisfactory relief of pain at their six-month postoperative visits. However, when this follow-up study was undertaken and a questionnaire sent out, 1 patient was three years after operation and the other seven, and both called the operation a failure and said that the dysmenorrhea had returned. Neither permitted reoperation to determine if regeneration had occurred, but that seems to be the best explanation. The infrequence of regeneration after this type of sympathectomy may be due to the fact that a long segment of nerve is removed, which so widely separates the nerve ends that they never rejoin. A reliable

test to determine the sympathetic supply to the uterus would be of help in this group.

The third possible cause of the failures is an inadequate sympathectomy. Seven cases were so classified because there was no other explanation. By history the dysmenorrhea was essential or primary. In 5 patients the estrogen test before operation completely relieved the pain, and yet presacral neurectomy was a failure. Sympathetic fibers may be missed at two places: the branches from the fourth lumbar ganglion to the presacral plexus often come from beneath the arteries rather than over the anterior surface, and these branches may be missed; more important is the chance of missing a large trunk that goes downward close to the inferior mesenteric and superior hemorrhoidal vessels. Elaut,[7] in a dissection of this area found that in only 25 per cent of the cases is the presacral nerve a distinct, single nerve. In 58 per cent there is a plexus lying between the common iliac arteries; in 16 per cent there are two parallel nerves, and in 2 per cent the nerve is arch shaped. In the last group the nerve may remain close to the inferior mesenteric vessels, and if the sigmoid is in a fairly free mesentery the presacral nerve may be retracted far laterally during the dissection and therefore missed. This anatomic variation may well account for some of the failures of this operation.

Pregnancy Following Presacral Neurectomy

Follow-up study on this group of 111 cases revealed the fact that 24 patients have had children since presacral neurectomy was performed. Since this operation successfully relieves menstrual cramps we were interested to see what effect the operation had upon first-stage labor pains. Of these 24 patients 8, or 33.3 per cent, experienced no severe cramps with uterine contractions and required no medication. These women and their obstetricians all commented on the lack of pain with labor. Several did complain of low back pain, and all noted the alternate hardness and softness of the uterus. Several patients experienced sensations other than pain with their contraction, such as a tingling sensation at the base of the spine. Two patients complained of discomfort in the rectum, and 1 of intestinal cramps. Two primiparas were delivered without obstetric assistance, since they had not thought that they were in labor until the vertex encountered the perineum. All the patients experienced pain with passage of the baby through the perineum, although this occurred so rapidly that post partum the patient complained of only one brief episode of pain. The force of uterine contractions was normal, and the obstetricians remarked that the labor seemed shorter than that of the average primiparous delivery. Of the 8 women with painless deliveries 6 had essential dysmenorrhea, and 2 had acquired dysmenorrhea due to endometriosis. Seven of the 8 had had complete relief of the dysmenorrhea by presacral neurectomy. In these 8 cases with painless deliveries the resection of the presacral plexus must have denervated the fundus of the uterus completely. The backaches described are probably due to dilatation of the cervix. Patients, therefore, who have had this operation should be warned that the first stage of labor may be painless and that the physician in charge should be notified when the uterus begins to contract regularly and forcefully.

Innervation of the Uterine Fundus and Cervix

Follow-up study also revealed the fact that although the relief of the crampy pains of menstruation was quite successful, 7 patients with essential dysmenorrhea continued to have backache with the periods. The backaches were not incapacitating. This fact that low abdominal cramps were relieved by presacral neurectomy and yet that the backache persisted aroused our interest in the innervation of the fundus and cervix. Pain from the uterus must pass upward in afferent fibers through the presacral plexus to reach the spinal cord. As with other visceral pain the actual pain felt by the patient is referred out along the sensory roots at the same level that the sympathetic fibers reach the cord. Theobald[8] believed that stimulation of the autonomic-nerve endings in the cervix caused a referred pain in the area of skin supplied by branches of the first lumbar nerve and that this pain should be abolished by local anesthesia to the skin area. Labor pain was also interpreted as being a viscerosensory, referred pain. Interruption of the presacral plexus by presacral neurectomy breaks this referred-pain arc. The work of Cleland[9] indicates that the afferent nerves from the fundus reach the cord at the level of the eleventh and twelfth dorsal segments. He found that nupercaine paravertebral block at this level relieved the pain of uterine contractions of women in active labor. Hingson[10] has confirmed this observation since he observed in 3000 cases that caudal anesthesia relieved the abdominal cramps of labor if the anesthetic included the eleventh dorsal segment.

In some women all the afferent fibers may go upward and through the presacral plexus from the cervix to the first dorsal and from the fundus to the eleventh and twelfth dorsal segments. However, since backache is often unrelieved by presacral neurectomy, the afferent nerve supply from the lower part of the uterus may pass outward through some other afferents. Anatomic dissections have shown that the parasympathetic supply to the uterus is from the second, third and fourth sacral segments. This fact may provide a good explanation of why the backaches associated with menstruation are unrelieved by presacral neurectomy and may also account for the backache that the women in labor had after presacral neurectomy, even though they experienced no cramps in 8 out of 24 cases.

Another bit of evidence that may point to variation in the innervation of fundus and cervix was presented by Meigs,[3] who did endometrial biopsies on 2 patients after presacral neurectomy and found that the passage of the curette through the internal os of the cervix caused backache but that scraping of the endometrial cavity caused no pain. He concluded that the cervix had not been denervated. Further studies are under way more accurately to map out the pathways from uterus and cervix to the central nervous system.

Endometriosis and Dysmenorrhea

We have been interested in searching for tiny areas of endometriosis in these patients with dysmenorrhea. Of the 89 patients with typical histories of essential dysmenorrhea 10 had tiny areas of endometriosis removed from the uterosacral ligaments or from the anterior surface of the uterus near the junction of the uterus and bladder. Endometriosis of this magnitude was only an incidental finding at operation and was not considered as an etiologic factor in the dysmenorrhea. Nine of these patients had complete relief of cramps after presacral neurectomy. In only 1 case to date has the endometriosis progressed. This patient had 90 per cent relief of cramps four years later but complained of sharp pain on the left side. Fixation of the left ovary suggested endometriosis. This observation of endometriosis in 11 per cent of patients with essential dysmenorrhea, whose average age was twenty-four years, makes it apparent that endometriosis may start at an early age. Whether women with essential dysmenorrhea are prone to develop endometriosis has not been ascertained from this study.

Dysmenorrhea Following Appendectomy

Included among the patients with acquired dysmenorrhea were 3 whose painful menstruation dated from an appendectomy. Tucker[1] had a similar group of patients, and presacral neurectomy for the dysmenorrhea relieved the cramps. No obvious cause was found at operation on these patients. The histories were very similar. The first patient had no pain with the periods, which had begun at the age of twelve, until she had a normal appendix removed at the age of nineteen. The periods grew steadily more painful postoperatively until a dilatation and curettage and presacral neurectomy four years later. No cause for the pain was found at laparotomy, and presacral neurectomy gave complete relief. In the second patient the periods had started at the age of fourteen and had been painless until appendectomy at the age of twenty. Thereafter severe cramps began two days before each period and continued for the first two days of the period until relieved by presacral neurectomy two and a half years later. No cause for the cramps was found at operation. In the third patient the periods had begun at the age of thirteen and had been painless until an appendectomy was done for chronic appendicitis at the age of twenty-two. After the operation severe cramps developed, starting one day before the onset of flow and lasting two or three days without let-up. At laparotomy six years later, a small endometrioma was found. The cramps were 90 per cent relieved by presacral neurectomy and resection of an endometrioma of the right ovary. A graduate nurse from this hospital gives exactly the same history of onset after appendectomy, having been free of pain prior to operation. This girl has refused presacral neurectomy. These cases are summarized to draw attention to the phenomenon of pain beginning after appendectomy. Fortunately, presacral neurectomy succeeded in relieving the dysmenorrhea.

Summary

A series of 111 cases of presacral neurectomy for dysmenorrhea are reviewed. Complete relief was obtained in 81 per cent of cases of essential and 52.6 per cent of acquired dysmenorrhea. There were 12 failures after presacral neurectomy for essential dysmenorrhea. These failures are accounted for on the basis of either regeneration of sympathetic nerves, incomplete operation or dysmenorrhea as a manifestation of a psychoneurosis. Twenty-four women had babies postoperatively; labor was painless for 33.3 per cent.

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PRIMARY FRIEDLANDER-BACILLUS PERITONITIS*

Report of a Case

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PRIMARY unexplained infection of the peritoneum by the Friedländer bacillus (*Klebsiella pneumoniae*) is a condition of evident rarity. The case reported below (the second in the medical literature) describes a disease that is a distinct though little known clinical entity. Additional reports will aid in delineating possible similarity to the better known idiopathic pneumococcal and streptococcal peritonitides of infants and children.

CASE REPORT

E. I., an 8-year-old girl of Irish descent, was referred to the hospital in April, 1943, by her family physician with the diagnosis of appendicitis with perforation. The immediate history dated to 4 days before admission, when she had complained of abdominal cramps and had vomited and retired to bed. There had been no stool for 3 days; the appetite had been very poor until the morning of admission, and since then the patient had eaten nothing. The abdominal cramps diminished somewhat after the 1st day, but on the day of admission returned with marked severity throughout the entire abdomen, and the child vomited several times. An enema was given on the afternoon before admission with slight relief from pain after expulsion of a small amount of gas. There had been some burning pain with urination on the day of admission.

The past history indicated no similar previous illnesses. The patient had been suffering from a fairly severe upper respiratory infection during the 2 weeks prior to admission. No previous symptoms could be referred to the gastrointestinal tract, urinary tract or gynecologic disorder. The patient had had measles and chicken pox in earlier childhood. A younger sister and the parents had been well during the period of the patient's illness. The remainder of the family history was noncontributory.

Physical examination showed the patient to be acutely sick, pale, listless and poorly oriented and breathing rapidly and complaining of generalized abdominal pain. The head was essentially normal. There was a very slight injection of the oropharynx; the tonsils were not remarkable. A few small, slightly tender lymph nodes were palpable in the neck, axillas and groins. The chest was clear, resonant and symmetrical and normal by roentgenogram. The abdomen was distended, tense and tender in all quadrants, especially the lower. No masses were palpable. There was tympany throughout. No peristalsis was audible. Rectal examination demonstrated tenderness in all directions, and withdrawal of the examining finger was followed by expulsion of gas and enema fluid.

The temperature was 103.8°F. by rectum, the pulse 140, and the respirations 28.

The white-cell count was 3600, with 64 per cent neutrophils, and, when repeated in 2 hours, 3200, with 56 per cent neutrophils. The hemoglobin was 68 per cent (9.5 gm. per 100 cc. of blood). Clear, bile-stained vomitus was guaiac negative. The urine was straw colored, clear and acid, with a specific gravity of 1.014, no albumin or sugar and no remarkable sediment.

A diagnosis of generalized peritonitis due to a perforated appendix or idiopathic pneumococcal infection was considered.

Immediate treatment consisted of placing the patient in an oxygen tent in restraints and allowing nothing by mouth except cracked ice. Codein phosphate (0.06 gm.) and sodium luminal (0.06 gm.) were given subcutaneously as often as needed for pain and restlessness. A Levine tube was passed into the stomach, which was emptied of a small amount of fluid, and was left for open dependent drainage. The patient was immediately given 1500 cc. of 10 per cent dextrose in physiologic saline solution with 2 gm. of sulfanilamide in solution as prontylin, and this was followed with 300 cc. of cross-matched citrated whole blood on the evening of admission. A Miller-Abbott tube (size No. 12 Fr.) was passed 25 cm. and was to be advanced; on the following morning the patient pulled the tube out, and it was not reinserted.

On the 1st hospital day the patient was listless and less well oriented than on admission and appeared to be in poor condition. A repeated examination of the blood showed 8.5 gm. of hemoglobin per 100 cc. and a white-cell count of 5100, with 54 per cent neutrophils. Operation under local anesthesia for drainage of pus from the lower abdomen and implantation of sulfanilamide was elected. A small right-lower-quadrant, muscle-splitting incision was made, and approximately 500 cc. of yellow, acrid-smelling fluid, of the consistence of thick broth, was expelled from the lower abdomen as though under pressure. A large rubber tube was inserted in the pelvis, and 8 gm. of crystalline sulfanilamide was implanted in the lower abdomen through the wound. This procedure was tolerated well.

The patient was treated on this and the 3 succeeding hospital days with continuous daily infusions of 2500 cc. of 10 per cent dextrose in physiologic saline solution, in addition to the infusion of 250 cc. of cross-matched citrated whole blood every 12 hours. The sulfanilamide level on the day after operation was 11.4 mg. per 100 cc., and thereafter sodium sulfadiazine in the continuous infusion was given in a dosage of 3 gm. per day. Sulfadiazine levels between 10.4 and 22 mg. per 100 cc. were subsequently recorded. The carbon dioxide combining power varied between 41.6 and 62 vol. per cent, and the urea nitrogen between 6.5 and 8.6 mg. per 100 cc. The hematocrit on the 3rd hospital day was 38 per cent. Hemoglobin determinations on the 1st, 2nd and 3rd days were 8.5, 10.5 and 10 gm. per 100 cc. of blood. The white-cell count mounted to 16,700, with 88 per cent neutrophils, by the 2nd hospital day but fell to 10,400, with 68 per cent neutrophils, on the 3rd day. The urine output was estimated to be satisfactory with at least 500 cc. each day. A culture of pus from the abdominal cavity at the time of operation grew out Friedländer bacillus in pure culture. A blood culture on the day of death was sterile.

Although some clinical improvement was noted in the hours immediately after operation, the patient's condition became progressively worse, and the temperature of 102°F. mounted to 104.8°F. 6 hours before death. The pulse mounted progressively to 176, and the respirations became more rapid, shallow and thoracic in character, remaining between 35 and 40 during the last 2 days. Signs of atelectasis and scattered coarse rales were noted during the last 2 days, and on the 4th hospital day the patient became comatose, aspirated vomitus and expired.

Autopsy. Post-mortem examination performed by Dr. Walter W. Brandes revealed a well developed and well nourished child weighing 25 kg. There was moderate cyanosis of the face and fingertips. The abdomen was moderately distended, and a recent 8-cm.-long McBurney incision was present.

The peritoneal cavity contained 1000 cc. of turbid fluid, with numerous soft, gray masses of exudate rich in fibrin. The peritoneal surfaces were hyperemic, and thick deposits of this exudate were present over them as well as over the upper surface of the liver. The appendix was also partly

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covered. No evidence of rupture or perforation of any viscus was found.

The pelvic organs showed peritoneal hyperemia and depositions of fibrinous exudate. The fallopian tubes were patent, and their lumens were free of exudate. The cavity of the uterus disclosed no evidence of inflammation. The ovaries were not enlarged.

Other organs demonstrated changes associated with marked inflammatory reactions. There was acute splenic swelling, parenchymatous degeneration of the liver and kidneys and passive hyperemia. Medullary portions of the adrenal glands were softened. The mesenteric lymph nodes were moderately swollen, soft and hyperemic. The small bowel presented only the serosal change mentioned. The mucosa of the cecum and ascending colon was noticeably swollen; it was soft, pale, and grossly edematous. There was no ulceration. The rectum was not noticeably altered. The pancreas was normal, and the gall bladder and bile ducts were not remarkable.

Examination of the pleural cavities revealed a small amount of fibrin present on the diaphragmatic surfaces. The thymus, mediastinum, great vessels, pericardium and heart were not remarkable. The trachea and major bronchi contained a small amount of gastric contents. Their mucosa was bluish red. The lungs revealed no gross evidence of pneumonia. They presented peripheral collapse, which was most noticeable in the lower lobes, more on the left side, involving two thirds of the left lower lobe.

Microscopical changes were those of an acute fibropurulent inflammation of the peritoneal surfaces. The exudate was composed of fibrin and leukocytes; fibrin predominated. Some of the polymorphonuclear cells were swollen and vacuolated. The subserosal layer of the peritoneal surfaces revealed marked hyperemia and edema, the edema sometimes extending to the submucosa of the bowel. There was no evidence of primary inflammation of the appendix, uterus, fallopian tubes or ovaries or of the gall bladder.

Cultures of the peritoneal exudate demonstrated a pure growth of Friedländer bacillus; contents of the lumen of the terminal ileum revealed the presence of this organism along with *Escherichia coli* and an unidentified member of the Clostridium group. A throat culture failed to demonstrate Friedländer bacilli.

Morphology of the cultures, cultural characteristics and morphology of the organism were those of Friedländer bacillus. Intraperitoneal mouse inoculations resulted in death after 12 hours, with demonstration of the organism in the peritoneal smear. Serologic typing of the organism (Julianelle) was not performed.

Discussion

The post-mortem examination failed to reveal the portal of entry of the infection or any primary site. Changes in the bowel, including the marked edema of the proximal colon, were, in all likelihood, secondary to the peritonitis. The presence of the infecting organism in the bowel lumen suggests that site as its source. In some unexplained manner the peritoneum became infected. Review of the literature disclosed a single case of probable primary peritonitis due to Friedländer bacillus reported in England by Cook[1] in 1931. As in the case presented above, the patient was a young girl (nine years old); she had an acute tonsillitis with exudate, and redness of the vagina, as well as generalized peritonitis when she was first seen five hours before death. This patient was treated by drainage of the lower abdomen performed under local anesthesia. Pus was described as dark and foul. Details of autopsy examination offered were throat and peritoneal culture (showing *K. pneumoniae*) and a description of a generalized peritonitis similar to that in the case presented above.

McDonald and Klingon[2] reported a case of peritoneal infection as "primary peritonitis caused by Friedländer's bacillus" in 1946, and considered it to be the first of such reports, apparently overlooking Cook's case. A review of their report leads to the conclusion that their case is not acceptable as a primary peritonitis of the etiology stated. The patient was a forty-seven-year-old man with a medically complicated past history and a recent history suggestive of a perforative lesion in the gastrointestinal tract. The patient was operated upon a few hours after the onset of an abdominal crisis; the culture of pus grew out not only a Friedländer bacillus but also beta-hemolytic anaerobic streptococci. The presence of a mixed bacterial infection, as well as certain other inconsistencies in the diagnosis, suggests that the case of Cook and the one reported above actually represent the only reported primary idiopathic infections of the peritoneum by the Friedländer bacillus.

Treatment

Aside from the merits of drainage vs. nondrainage and intraperitoneal use of sulfonamides, rational therapy for this condition with means now at hand must be predicated on early diagnosis. Only thus may suitable surgery be employed and the most likely antibacterial agents used. The technic reported by Ladd and Gross et al. as used at the Children's Hospital, Boston, with diagnostic smear of peritoneal exudate obtained by early laparotomy, would accomplish differentiation of the Friedländer bacillus from the streptococcus, pneumococcus and the mixed infection of fecal peritonitis. The Friedländer bacillus is easily recognized as an encapsulated, short, plump, gram-negative rod and is present in large numbers in exudates of peritoneal infection so caused. Characteristic encapsulation is striking in these smears and is easily seen with ordinary aniline (dye) stains.

Studies and reports in recent years have indicated that sulfadiazine is probably the most effective sulfonamide drug for use against the Friedländer bacillus. Sesler and Schmidt[3] have shown clearly that this is true both in vitro and in animal experiments, although the variation in reaction of different strains of the organism is emphasized. Ransmeier and Major[4] assembled comparative statistics of mortality to show that sulfadiazine improves the outlook in the highly fatal Friedländer meningitides. Heilman[5] and others have shown that streptomycin may be more effective than any other antibacterial agent.

Penicillin is not effective in physiologically feasible concentration. However, Heilman and others found such variation in sensitivity to streptomycin (four thousand times the original concentrations in vitro) of different strains that one must conclude that some cases cannot be benefited by streptomycin administration. When possible, preliminary assay of the effect of either sulfadiazine or streptomycin in vitro

would aid in anticipating the most successful treatment. Serologic and bacteriologic classification of the organism is of no value, since there is no correlation between type and either sensitivity to sulfadiazine and streptomycin or virulence and occurrence as a pathogen. Organisms are most often Julianelle Type A, but virulent infections are also caused by types B and C and those of Group X.

Bacteriology

The Friedländer bacillus is grossly related to the coliform group. It is known to be a common organism of the bacteriologic flora of the intestinal tract. Kendall,[6] whose study seems to have included *Aerobacter aerogenes* as well, found that these organisms were common in the intestines of infants but not in those of adults, whereas Dudgeon[7] cultured the organisms in the feces of 5.5 per cent of a large group of patients, most of whom had some lesion or disease of the oropharynx or of the intestinal tract. Baehr, Schwartzman and Greenspan[8, 9] state that it is a more frequent inhabitant of the intestine than elsewhere and is rare as a primary pathogen in the respiratory tract, where it usually appears as a secondary invader. Most textbooks of bacteriology state that this organism is found chiefly in the respiratory tract in man. The Mt. Sinai workers, however, report a unique and significant study of 61 cases of peritonitis caused by this organism alone or in conjunction with other organisms; in all these cases the portal of entry was demonstrated (mostly perforated appendix or bowel). The authors further described abdominal infection from liver abscess and biliary-tract, urinary-tract and pelvic infection, so that of 198 consecutive cases reviewed, 163 infections due to the Friedländer bacillus were present in the abdomen, pelvis or urinary tract. This report has stimulated comment[10] and greatly clarifies the understanding of the pathogenesis of infections due to the Friedländer bacillus.

After Friedländer[11] described the organism that bears his name as the virus causing lobar pneumonia (from post-mortem lung cultures in 8 cases) and designed it as "*Klebsiella pneumoniae*," the error of his conclusion was soon demonstrated by description of the pneumococcus as the far more common pathogen in such cases. However, even now the term "pneumobacillus" is a common synonym for the official (Bergey) *K. pneumoniae*. It has been suggested that the long-delayed recognition of the true natural occurrence of the Friedländer bacillus as a pathogen may be due in part to cultural and morphologic similarity to the colon bacillus, because of which in modern rapid hospital bacteriology the Friedländer bacillus is often reported as *Esch. coli*, and to the larger attention accorded culture and other bacteriologic study on medical wards (and in cases of chest infection) than on surgical patients (with perforative lesions of the gastrointestinal tract).

In this connection, the excellent studies of Osterman and Rettger[12, 13] on comparison of the organisms of the Friedländer and coli-aerogenes groups are cited. These authors indicate that, whereas there may occasionally be erroneous identification by ordinary biochemical reactions and cultural characteristics (in particular when virulent nonencapsulated forms of Friedländer and Aerobacter organisms or colon bacilli that are encapsulated are encountered), no valid criteria exist for the differentiation of the organisms that can be applied consistently to all cases. The authors state that there has been a tendency to rely on the origin of a culture as a material aid in its identification and point out that in their study, cultures of *Esch. coli* and *A. aerogenes*, as well as the Friedländer bacillus, came from similar and diverse natural sources. They consider that further study by serologic means will provide a more complete explanation of interrelations.

Examination of the bacteriology in reports cited reveals that in Cook's case, only a statement that the cultures showed a Friedländer bacillus is offered; in the case reported above, the morphology, mouse virulence and biochemical characteristics (admittedly variable) were the basis for identification; and in the series of Baehr, Schwartzman and Greenspan, the criteria were "Gram negative bacilli showing well defined capsule and typical 'gum drop' and stringy colonies on solid media were considered to belong to the *B. friedländer* group, provided these characteristics persisted for at least three to four passages through artificial media." Thus, the certainty that these authors were not in some cases dealing with *A. aerogenes* is by no means established.

Ostermann and Rettger believe that serologic typing is most conclusive in identifying strains of Friedländer bacillus that can be so treated, and studied the antigenic relation of the Friedländer bacillus, *A. aerogenes* and *Esch. coli*. They emphasize the occurrence of variation in colonial morphology, group antigenic relation and the exceptions that seem to occur when any set of standards for identification are applied. The problem awaits further elucidation, even to the study of the normal and pathologic occurrence of the Friedländer bacillus, identified with means now at hand.

If the findings of the Mt. Sinai workers can be substantiated in the light of these conditions, amendment to the older teaching that Friedländer-bacillus infections occur most commonly above the diaphragm and redesignation of the organism as either *Bacillus friedländer* or *B. mucosus capsulatus* are suggested. The list of primary infections caused by this organism gleaned from the literature includes those in the sinus, mastoid and middle ear, throat, lungs, heart, pericardium and intravascular sites, peritoneum, biliary tract and liver, perinephric space, kidneys and lower urinary tract, pelvic organs of the female, and prostate, vesicles and epi-

didymis of the male, brain meninges, bone and soft tissues of the extremities.

Summary

A case of primary generalized peritonitis due to the Friedländer bacillus, the second in the medical literature, is reported.

Some aspects of the treatment of such infection with newer agents are briefly discussed.

Attention is again directed to the similarity in occurrence and pathogenicity of Friedländer bacillus and *Escherichia coli* and to the probable error of considering the Friedländer bacillus to be primarily a pathogen in the respiratory system. The problem of bacteriology and identification is discussed.

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MEDICAL PROGRESS

ABDOMINAL SURGERY (Concluded)

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The Duodenum

Shapiro and Robillard[61] discuss anomalies of the blood supply of the duodenum. There are many variations in the vascular arrangement in this region, and unless these are recognized, avascularization of the duodenal stump following gastrectomy may result in necrosis and leakage. Avoidance of this complication is simple if the surgeon frees the duodenum from the pancreas only enough to allow an adequate turn-in of the duodenal stump. This is best accomplished if the adherent and inflammatory area about the ulcer site is approached after the stomach has been transected. Freeing the duodenum distal to the ulcer as a first step in the procedure is more apt to lead to avascularization with subsequent necrosis.

Ferguson and Cameron[62] advise giving the patient with a diverticulum of the duodenum a drink of barium the night before operation. The barium coats the lining of the diverticulum, making it easier to find. They point out that such lesions are a herniation through the muscular coat of the bowel and occur usually on the mesenteric border between two blood vessels. They recommend free dissection and inversion of the diverticulum, repairing the defect in the musculature with interrupted fine silk sutures.

Mahorner and Kisner[63] suggest the inflation of the duodenum with air introduced through a 22-gauge needle on a 20-cc. glass syringe, to outline diverticula. They advocate free dissection and amputation distal to a small clamp applied to the neck of the diverticulum. The mucosa is inverted with a 00 chromic catgut suture, and the muscularis with interrupted fine silk or cotton sutures.

All the authors cited above agree that the incidence of diverticula of the duodenum is from 1 to 2 per cent of the adult population. The majority of these lesions are symptomless or cause dyspepsia easily controlled by dietary measures. A small percentage of patients may have sufficient disability to warrant corrective surgery.

Acute perforation of duodenal ulcer is again discussed by Graham.[64] In 125 consecutive cases treated at the Toronto General Hospital the operative mortality was 6.4 per cent. The author considers chemical and nutritional imbalance, rather than bacterial peritonitis, to be responsible for the serious shock-like state of the patient after perforation. He believes that better results can be obtained if the patient in poor condition is given supportive therapy for a few hours prior to surgery. Attention is called to nature's tendency to seal the

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perforation by a deposit of fibrin. He stresses the importance of aiding this process by the application of a tab of omentum to the area. Concomitant gastroenterostomy, gastroduodenostomy, gastric resection, intraperitoneal use of sulfonamides and drainage of the abdomen are all condemned.

Bohmansson[65] has presented an excellent discussion of massive hemorrhage from peptic ulcer. The problem is a combined one that concerns the internist as well as the surgeon. Careful evaluation of such cases should be made to determine whether or not conservative or radical treatment is indicated. Early operation is advocated if the roentgenogram shows a crater or if there is a history of previous perforation or if the ulcer is known to be chronic and when shock-level bleeding cannot be readily combated by blood transfusions. Radical operation is recommended if any surgery is done, since this is the only feasible approach to blood vessels leading to the ulcer area, and exact hemostasis is necessary. By the combined efforts of medicine and surgery, the mortality was reduced from 9.1 per cent in 1939 to 5.1 per cent in 1945. The operative cases were decreased during this period from 45 to 7 per cent of the total. The mortality of the conservatively treated group was reduced from 6 to 5 per cent, and the operative mortality fell from 13 to 5.1 per cent.

Heuer[66] reports that 8 per cent of 337 patients admitted to the New York Hospital with acute massive bleeding from peptic ulcer died. Fifteen per cent of the cases were of the type that would have resulted fatally had not operative interference been carried out. He stresses early decision for or against surgical intervention. The mortality was 10 per cent in patients operated on early in the episodes, as compared with 70 per cent when the operation was undertaken after several days of bleeding. He also emphasizes the necessity for radical gastrectomy in these cases, stating that palliative operations are useless.

There is some tendency to operate early in more cases of acute massive bleeding from gastric and duodenal ulcer than formerly. With the marked reduction in the operative risk now evident, there is a definite argument in favor of such an attitude. The fact that the younger patients in this group almost invariably cease to bleed under conservative treatment, whereas the older patients more frequently died of hemorrhage during the episode, has been stressed.[67] So far, surgeons have not been able to bring about a successful outcome very often if the operation is undertaken after several days of bleeding. It is true that most of the patients operated upon within seventy-two hours of the onset of hemorrhage can be brought through safely. Much time could be saved the younger patients by a radical attack as soon as shock had been properly controlled, since most of them should be operated upon eventually to prevent recurrences of these disturbing bouts of bleeding.

Dragstedt et al.[68] express their present attitude concerning transabdominal vagus resection for ulcer. Sixty-one transthoracic and 109 transabdominal vagotomies form the basis of their thesis. They also confirm previous reports that the vagus nerves have several anatomic variations but believe that all these cases lend themselves to the abdominal approach. They have no hesitancy in combining vagotomy with gastroenterostomy or gastroduodenostomy when there is evidence of cicatricial obstruction. Eighteen out of their total of 170 cases showed evidence that the vagi had not been completely interrupted. Reoperation with resection of retained vagus fibers resulted in relief in 2 patients. Six of the 18 had recurrence or persistence of ulcer symptoms. The patients were maintained on gastric suction for from four to six days after vagotomy, and a normal diet was not tolerated for from two to eight weeks.

Fallis and Warren[69] state that anastomotic ulcer occurs in 15 per cent of patients having gastroenterostomy for duodenal ulcer. The stomal ulcer always occurs in the efferent loop of jejunum opposite the anastomosis. Patients who have had perforation or bleeding from the original ulcer are prone to have the same manifestation in the new lesion. The authors consider medical treatment unsatisfactory for these patients and, at the time of their report, believed that subtotal resection of the stomach, with aseptic technic and short-loop retrocolic anastomosis, was the treatment of choice.

The Small Intestine

Pemberton and his associates[70] bring to mind the rare lesion described by George Whipple in 1907, termed "lipodystrophy." They believe that only 14 cases have so far been reported and add 3 cases observed at the Mayo Clinic. The syndrome in brief is that of abdominal pain and weight loss, a doughy-feeling mass in the abdomen and steatorrhea. The findings are those of mesenteric thickening with engorged lymphatic vessels. Microscopical examination of the fatty tissue of the mesentery shows leukocytes and giant cells. X-ray and bile-salt therapy has been suggested but is of questionable value. The usual course is one of long duration and gradual disintegration.

Lazarus and Marks[71] discuss benign intestinal tumors of vascular origin, finding 38 cases reported in the literature. These tumors vary from capillary nevi to cavernous hemangiomas. It is probable that some of the cases of obscure gastrointestinal bleeding can be accounted for on the basis of these lesions which are often small and easy to overlook. The authors describe a patient who continued to bleed after four operative attempts had been made to remove the vascular tumors, which are often multiple and may involve the entire intestine.

Saltzstein and Rao[72] report the history of a patient who bled massively from the intestine. Exploration revealed a surgical sponge, which was encysted but had eroded a 1-cm. area of the ileum. The patient had been operated on twenty-five years previously for a pelvic complaint and twenty-three years before for intestinal obstruction. The authors quote Crossen and Crossen,[73] who collected 250 cases of foreign bodies in the abdomen, as stating that these usually gravitate to the pelvis and become extruded through the bowel, vagina or bladder. Fourteen of the 250 foreign bodies had remained within the abdomen for five or more years, and these were all encysted.

A case of leiomyoma of the jejunum operated on for massive hemorrhage supposedly from duodenal ulcer is reported by Marshall and Welch.[74] The lesion was located 15 cm. beyond the ligament of Treitz and was successfully resected.

Botsford and Seibel[75] have reported all the tumors of the small intestine, exclusive of those arising from the papilla of Vater and the pancreas, encountered at the Peter Bent Brigham Hospital, Boston, from 1913 to 1946. Sixty-five primary tumors were found, of which 33 were malignant and 32 were benign. The malignant tumors were classified as adenocarcinoma in 18, lymphosarcoma in 13 and carcinoma in 2 cases. The benign lesions were lipomas, adenomas, leiomyomas and fibromas in that order of frequency. There were 10 in the duodenum, 14 in the jejunum and 41 in the ileum. Half the lesions were apparently symptomless and were found incidentally. The observations are in accord with the experience of others that adenocarcinoma is more common in the high intestine and that sarcoma is more often found in the ileum.

Rabinovitch et al.[76] found 15 cases of sarcoma of the bowel in the records of the Jewish Hospital, Brooklyn, New York, in a twenty-five-year period. They state that this lesion has a ratio to carcinoma of 1:5.5 in the small intestine, 1:275 in the colon and 1:577 in the rectum.

Patent omphalomesenteric duct and its relation to the diverticulum of Meckel is discussed by Kittle and his co-workers,[77] who present an excellent review of the history and embryology of this lesion. Although Meckel's diverticulum occurs in from 1 to 2 per cent of the populace, a patent omphalomesenteric duct has been reported in only 128 cases. The authors cite 3 cases of their own and call attention to the importance of the lesion in producing intestinal obstruction when a loop of small intestine prolapses through the patent ductus. For this reason, they advise operative correction of this congenital defect whenever the diagnosis is made.

Another good review of the literature on Meckel's diverticulum has been made by Haber.[78] He studied critically 23 case histories at his disposal and emphasized the significance of this lesion in the differential diagnosis of patients with apparent intestinal obstruction.

Devine[79] presents an excellent discussion of paralytic ileus. From the study and observation on 43 cases, he deducts that this syndrome can be divided into three stages. In the first stage, there is normal bowel activity, and the intestine can respond to stimulation. During the second stage, there is disordered movement and drugs that stimulate peristalsis, as well as enemas, will do no good but will increase discomfort and distention, thereby hastening the third stage. In this last phase, there is loss of intestinal motility with the development of full-blown ileus. Experiments following intestinal intubation with various local applications and drugs led to these concepts. Heat and turpentine stupes had no effect on bowel movements. Barbiturates decreased peristalsis and bowel tone. Penicillin and sulfonamides did not affect motility. Overdistention of the stomach produced loss of bowel tone and movement. Stimulation of the colon with enemas also stimulated the small intestine. Devine advises no cathartic before operation, gentle handling of the intestine, limitation of fluids by mouth for twelve hours postoperatively because of swallowed air, atropine and barbiturates to be kept to a minimum, the liberal use of morphine and no stimulation of the intestine by drugs or enemas until peristalsis is normal. Miller–Abbott intubation and intravenous fluids offer the best treatment for paralytic ileus when it occurs.

Watt and Harner[80] report 3 cases of intestinal obstruction from bezoars. Two of these were from the ingestion of persimmons, and the other from hair. All were found in the terminal ileum, and all the patients recovered after surgical removal of the bezoars.

An interesting case of intestinal obstruction from the rapid ingestion of five oranges in a man with a previous Polya operation is reported by Baumeister and Darling.[81] The orange pulp had collected in the ileum and had to be removed surgically to relieve the obstruction. I have encountered a similar case in an edentulous man with a previous gastroenterostomy who admitted swallowing a peeled orange in two halves. At operation it appeared that these sections had come together and lodged in the usual narrow area of the terminal ileum.

Eliason and Welty[82] review the records of cases of intestinal obstruction at the University of Pennsylvania Hospital in a period of ten years. Patients treated before the Miller–Abbott tube was used gave a mortality rate of 50 per cent, as compared to 11 per cent in recent years. The average age of the survivors was forty-four years, and that of those who died was fifty-nine years. The mortality in patients with cancer was 34 per cent; in strangulated femoral hernia, it was 31 per cent, and in strangulated inguinal hernia, it was 5 per cent. Excluding cancer

and strangulation obstruction in 159 consecutive cases, there was 1 death in the recent series.

Seven children with strangulated, nonreducible intussusception were treated by resection and primary anastomosis by Dennis,[83] with no deaths. He advocates end-to-end anastomosis with one row of silk Halsted mattress sutures, and points out that the inflammatory reaction occurring about catgut sutures may well account for edematous obstruction and failure.

Retrograde intussusception is discussed by Thorek and Lorimer.[84] They report a case of a fifty-nine-year-old Negress who developed a gradual obstruction from an adenocarcinoma of the cecum. At operation the cecum was invaginated into the terminal ileum, which was dilated to one and a half times the size of the transverse colon. They quote Groper's[85] classification of retrograde intussusception as follows: jejunogastric, enteric, cecoileal and colic.

Garlock[86] has analyzed 200 cases of regional ileitis treated at the Mt. Sinai Hospital, New York City. The acute phase of the disease is nearly always diagnosed and operated on as acute appendicitis. The patients do surprisingly well, and in many cases the disabling chronic phase of the disease does not follow. If remissions last for a number of years after an acute onset, the patient rarely has a recurrence. Although some patients with chronic cases do well on conservative measures and are not disabled by the disease process, the majority of them develop fever, weight loss, fistulas and abscesses. This tendency makes it justifiable to consider them as primarily a surgical problem. Ileotransverse colostomy, following a division of the ileum with closure of the distal segment, gives the best results. There was no mortality after this procedure, and only 10.5 per cent of patients developed recurrences requiring resection of the terminal ileum and right portion of the colon. Ileocolostomy in continuity not only failed to improve these patients but also made them worse. One-stage resections were associated with a mortality of 16.3 per cent and recurrences of 15.4 per cent. Two-stage resections resulted in 12 per cent mortality and 28.6 per cent recurrences. Garlock believes that the disease starts in the ileum and not in the lymphatic vessels. He calls attention to the fact that fistulas close spontaneously after they are excluded by ileotransverse colostomy.

The Colon

Beck and Hopkins[87] report 5 cases of diverticulitis of the cecum. Four patients had acute manifestations and were operated on with the diagnosis of acute appendicitis. Two were treated by simple resection of the diverticulum, 1 by right colectomy and primary ileotransverse colostomy, and 1 by a resection of the Mikulicz type. One case was diagnosed preoperatively, and the diverticulum excised after a planned cholecystectomy.

Two cases of diverticulitis of the cecum and ascending colon are reported by Fairbank and Rob.[88] They discuss the difficulties in differentiating these lesions clinically from carcinoma. Both patients were treated by right hemicolectomy with recovery.

Anderson[89] reviews this subject and finds 91 reports of acute diverticulitis of the cecum in the surgical literature. Diverticula in the colon are found in 5.7 per cent of roentgenograms and 6.9 per cent of autopsies at the Mayo Clinic. In 700 cases of surgical diverticulitis treated there, only 9 were in the right portion of the colon. Eight case histories are given in the report. Resection of the right portion of the colon or cecum had been carried out in one third of the cases, probably because they could not be distinguished from perforated carcinoma. The preoperative diagnosis in 84 of the 91 cases reported was acute appendicitis. The operative mortality in the whole group was 6.4 per cent. Local procedures when they could be done carried less risk than bowel resection. The average age of these patients was thirty-nine years and two months. This is striking, since the more common sigmoid diverticulitis is found in a much older age group.

Pemberton et al.[90] have reported the results obtained in the surgical treatment of 389 patients with diverticulitis of the sigmoid colon. Two hundred and forty-five of these were treated between 1908 and 1940, with a mortality of 14.7 per cent. One hundred and forty-four were treated from 1941 to 1945, with a mortality of 4.2 per cent. The authors deduce from their experience that proximal colostomy should be done in all acute cases. They advise resection of the diseased area by the Mikulicz principle six to twelve months later. They attribute the better results obtained in the second group of patients largely to the use of sulfonamides.

Scott and Serenati[91] have analyzed the records of 31 patients with megacolon occurring in 250,000 admissions to the Strong Memorial Hospital, Rochester, New York. These cases are divided into four categories: neurogenic; congenital with organic obstruction; functional with obstruction; and those with extrinsic metabolic effects such as avitaminosis, malnutrition and hypothyroidism. The congenital obstructions are relieved surgically without further consideration. Conservative measures are carried out in all other cases. Parasympathetic drugs, enemas and mineral oil are given a thorough trial. Spinal anesthesia may bring about a dramatic temporary effect, and when this occurs, sympathectomy is indicated. In some cases, in which there seems to be a more lasting effect from spinal anesthesia, a continuation of conservative treatment justified. If colectomy is done, the authors advise only a left hemicolectomy and a lateral anastomosis to produce the widest possible stoma.

Young and his associates[92] report 7 cases of volvulus of the cecum, which they consider to account for slightly more than 1 per cent of all cases of intestinal obstruction excluding external hernia. The authors believe that the diagnosis can often be made by a typical appearance observed in the scout roentgenogram of the abdomen. A carefully given barium enema may be necessary to confirm the diagnosis. If the lesion is early and the bowel viable, detorsion and cecostomy are advised. The fixation of the cecum by inflammatory reaction about the cecostomy prevents recurrence. Resection must be done if vascularity of the bowel has occurred. Exteriorization of the Mikulicz type is usually the safest procedure in such cases.

Volvulus of the sigmoid colon is discussed by Bruusgaard,[93] who states that this condition is much more common in the eastern European countries than in western Europe and the United States. He attributes this to the high vegetable diet, particularly during the war years, necessary in eastern Europe. Apparently volvulus of the sigmoid accounted for from 30 to 50 per cent of intestinal obstructions in these countries as compared to 10 per cent in the United States. Ninety-one patients with this lesion were treated in the Ullevaal Hospital, Oslo, in a ten-year period. Fifty-seven of these were over sixty years of age, whereas only 4 were under forty. The diagnosis was made by the characteristic symptoms and scout films of the abdomen. When there was fever and leukocytosis, the assumption of vascular disturbance led to immediate laparotomy and exteriorization of the bowel. If the patients had no signs or symptoms of necrosis, they were sigmoidoscoped and relieved by the passage of a soft-rubber rectal tube into the distended twisted segment of bowel. This method was successful in 123 cases. Recurrences accounted for the fact that the 91 patients had a total of 168 admissions to the hospital. If elective surgery was carried out, it was done in four stages, as follows: cecostomy, followed by exteriorization of the sigmoid with later operative closure, and finally closure of the cecostomy.

Guptill[94] has collected from the literature 347 cases of familial polyposis of the colon. He adds 5 cases occurring in two families that he has encountered. Very low ileorectal anastomosis with colectomy in stages is recommended. Polyps in the retained rectum must be treated by fulguration when they are found on regular examinations. The intervals of these inspections may vary from one to six months, depending on the rate at which new polyps develop. Guptill calls attention to the advisability of careful examination of all members of such families. Even those who do not have polyposis are prone to develop carcinoma of the colon on the basis of a single polyp.

The evolution of adenomas of the large intestine and their relation to carcinoma are discussed by Helwig.[95] His report is based on 1460 consecutive autopsies in which 139 subjects, or nearly 10 per cent, had adenomas of the colon. Twelve of these revealed cancer on microscopical examination. He states that adenomas are true tumors and are not based on previous inflammation. The incidence was greater in white persons than in Negroes. Also, it was greater in men than in women. The incidence increased with age, and 24 per cent occurred in the eighth decade of life. The average number of adenomas found was two per subject, although 58 per cent revealed a single lesion.

Bartlett[96] reviews the results of treatment of 298 colostomies in an Army hospital center. He advises meticulous removal of all scar tissue of the skin, fat, fascia and bowel, followed by an accurate suture of the bowel, which is dropped free into the peritoneal cavity. Careful wound closure is then accomplished. There was only 1 fatal case in the 298 closures, which included 60 end-to-end anastomoses.

An ingenious and effective method of preparing the obstructed colon is reported by Millet.[97] A large rubber-tube cecostomy is done after a modification of Gibson's technic. Twenty-four hours later, a small opening is made into the anterior wall of the tube. Through this is passed a Miller-Abbott tube, which is carried by peristalsis gradually to the point of obstruction. Irrigation can then be successfully carried out through the long double-lumen tube. The bowel proximal to the obstruction can thus be thoroughly cleansed in four or five days.

Ochsner and Hines[98] analyzed the records of 113 consecutive cases of carcinoma of the colon coming under their care. Ninety-six of these patients, or 84.8 per cent, had resections as follows: 18 right colectomies, with no deaths; 56 left colectomies, with 2 deaths; and 48 rectosigmoid, usually by combined abdominoperineal operations, with 2 deaths. The resectability was highest in the rectosigmoid group. The authors stress the danger of recurrence when continuity is attempted in patients with low and extensive lesions.

Experience with cancer of the colon at the Massachusetts General Hospital has been brought up to date.[99] The resectability rate was 95 per cent in the last group of cases, as compared to 91 per cent in a former series. Primary anastomosis is done in all cases except those requiring combined procedures. An outer row of fine cotton and an inner row of fine catgut sutures are used in an open anastomosis. Obstructed cases have preliminary cecostomy, and if this is not effective, transverse colostomy is done. All patients are treated for from five to seven days with 8 gm. of sulfathaladine daily before operation. Secondary wound closure is practiced. The mortality rate has been greatly reduced, largely owing to better preparation, anesthesia, blood replacement and antibiotics.

Johnston[100] has collected from the literature 48 cases of carcinoma of the colon occurring in children under sixteen years of age. He reports a case of colloid carcinoma of the right portion of the colon in a three-year-old child. He states that colloid carcinoma is ten times as frequent in children with cancer of the colon as it is in adults.

Gilchrist and David[101] have reviewed 200 cases of carcinoma of the colon and rectum operated on more than five years before. The operability rate for this period was 75 per cent, and the operative mortality was 9.5 per cent. One hundred and twenty-five patients had lymph-node metastasis. One hundred and fourteen patients, or 57 per cent, were alive and apparently well five or more years after operation. Eight patients died during the five-year period of causes other than recurrent cancer. Seventy-eight and five tenths per cent of the patients who survived for five years had no lymph-node involvement at the time of operation, whereas 44.8 per cent of those with lymph-node involvement lived five or more years. The survival rate was somewhat greater in the intraperitoneal than it was in the extraperitoneal lesions. The right portion of the colon was more favorable for cure than the left. In 35 patients with resectable extension of disease to other structures, 14 were alive and well five or more years after operation. In 11 autopsies done on patients failing to survive operation, residual positive lymph nodes were found in 4.

A ten year follow-up study on 337 patients with cancer of the colon and rectum has been presented by Colcock.[102] Of 103 cases of cancer of the colon, 81 (78.6 per cent) were resected. The operative mortality in this group was 16 per cent. The Mikulicz type of resection was generally used. Of 38 patients without lymph-node involvement, 5 died in the hospital, and 5 died of unrelated disease afterward. Of the 28 remaining in this group, 18 were well at the end of five years, 2 died of recurrence between the fifth and tenth years, and 16 were well at the end of ten years. Of patients who survived operation in this group, 64.3 per cent lived five years, and 57.1 per cent lived ten years. In 27 cases with extension of disease, 8 died after operation, 15 died of recurrence within five years, 1 died of recurrence after five years, and 3 were alive and well after ten years. The results on cancer of the rectum and rectosigmoid were better. There were 60 per cent five-year and 51.6 per cent ten-year survivals in cases considered favorable at the time of operation, although in the unfavorable group, there were 30.2 per cent five-year and 23.2 per cent ten-year respites. The report of Gilchrist and David[101] is on a slightly different basis, and this may account for the apparent variation in results in these two important contributions.

Mider[103] gives an interesting analysis of 726 cases of carcinoma of the colon in which 21 patients had multiple carcinomas in the bowel, 17 cases being found at the first operation and 4 appearing later in life. Adenomatous polyps were found in 8 patients elsewhere in the colon but more usually near the site of the cancer. Seventeen per cent of the patients with single cancers had polyps as well, and 38 per cent of those having multiple malignant lesions had polyps elsewhere in the bowel.

Dunphy[104] has reported the results obtained in reoperation in 4 patients with recurrent carcinoma of the colon. These patients seemed to have local recurrence only, without evidence of extension to the liver and so forth. They enjoyed long respites after bloc excision of these recurrent lesions, which often involved neighboring but nonvital structures. In an attempt to explain the local rather than distant metastases, it appeared that these lesions were originally associated with inflammatory processes. Dunphy reasoned that the lymph channels leading from the area might have been previously blocked by inflammation, which led to the gradual development of remediable local recurrence.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 34111

PRESENTATION OF CASE

First admission. A fifty-eight-year-old man was admitted to the hospital with progressive weakness and malaise.

Four months before entry he noticed weakness and fatigue, which at first he attributed to overwork. Two months later he developed a sharp pain in the right loin, which was worse on deep inspiration. This was soon followed by cough with copious yellow sputum and a temperature of 102°F. Aspirin was given, and the right side of the chest was strapped, with slight improvement. He was then given sulfadiazine for nine days, and the temperature fell to normal but rose again after the drug was stopped, fluctuating between 99 and 102°F. There were no actual chills. Two weeks before admission he experienced a sharp severe left-upper-quadrant pain, which came on suddenly and was made worse by deep inspiration. It was accompanied by nausea, vomiting and increased fever and required morphine for relief. The pain gradually subsided over several days.

A heart murmur had been discovered on routine physical examination twenty-five years previously and had again been noted two years before entry. There was no history of rheumatic fever.

Physical examination revealed a poorly nourished man, with pale dry skin and café-au-lait spots over the abdomen and extremities and several petechiae over the anterior surfaces of the legs. There was slight ankle edema. The heart was questionably enlarged. There were harsh systolic murmurs at the apex (Grade I) and at the base (Grade III). The aortic second sound was slightly greater than the pulmonic. There were a few moist rales at the right base. The spleen was very large, 11 cm. down in the nipple line, hard and moderately tender. The liver was not definitely enlarged.

The temperature was 101°F., the pulse 88, and the respirations 22. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood disclosed a red-cell count of 3,000,000, with a hemoglobin of 11 gm., and a white-cell count of 3300, with 58 per cent neutrophils and 42 per cent lymphocytes. The serum nonprotein nitrogen was 41 mg. per 100 cc., the total protein 7.2 gm., and the chloride 102 milliequiv. per liter. The urine was loaded with red cells. Blood cultures were negative. An x-ray film of the chest showed partial collapse of the left upper lobe, with many areas of increased density and emphysematous blebs in the left apex. There was no infiltrative lesion. The heart and great-vessel shadows were normal. A plain film of the abdomen showed proliferative changes in the lumbar spine and a soft-tissue mass in the left side of the abdomen. An electrocardiogram was within normal limits.

The patient was started on penicillin, 500,000 units daily, later increased to 1,000,000 units and then to 2,000,000 units a day. After sixteen days of this therapy he was still having a low-grade fever and had developed an area of cellulitis at the site of the eight-day intramuscular constant penicillin drip. The drug was accordingly stopped, and blood cultures were pursued with renewed vigor without

success. Two sternal-marrow aspirations were also negative on culture. He was given four transfusions of 500 cc. of blood each.

One month after admission he developed diarrhea, nausea and left abdominal pain. Examination revealed slight tenderness over the spleen and a slightly high-pitched hypoactive peristalsis, and there were new petechiae over the legs. He was then put on penicillin, 10,000,000 units intramuscularly a day in 800 cc. of physiologic saline solution for four weeks with no response. During that time the white-cell count was 2500 to 8000, the hemoglobin 9.5 to 13.5 gm., the serum nonprotein nitrogen 35 to 40 mg. per 100 cc., the total protein 6.1 to 7.4 gm. with an albumin-globulin ratio of 0.9, the carbon dioxide 24 milliequiv. and the chloride 100 milliequiv. per liter; the cephalin flocculation reaction was +++ in twenty-four hours. The bromsulfalein test showed 18 per cent retention of the dye in forty-five minutes. The prothrombin time was normal. Repeated blood cultures (thirty-one in all) were still negative. The blood penicillin level was between 9.14 and 0.6 units per cubic centimeter. The urine consistently showed profuse hematuria and +++ test for albumin, the specific gravity ranging from 1.005 to 1.012. The stools were negative.

Two months after admission the patient developed ascites, and the venous pressure in the right arm was equivalent to 6 cm. of saline solution. Two weeks later he had tenderness in the right calf, with some enlargement of this area, but a negative Homans's sign and absence of increased heat or dilated superficial veins. On the following day he had bilateral ankle edema, nausea and vomiting, restlessness, and pain in the anterior left portion of the chest and precordium, exaggerated by respiration. The heart rate was 100 per minute, and there was a gallop rhythm. The blood pressure was 158 systolic, 108 diastolic. An electrocardiogram showed no significant change, and a chest film revealed fluid in the right base and prominent lung roots. He was then given 0.1 gm. of digitalis daily, and after a week the gallop rhythm disappeared and the edema subsided. A thoracentesis yielded 575 cc. of straw-colored fluid. A biopsy of the deltoid muscle showed a small focus of degeneration with lymphocytic and monocytic infiltration. A tuberculin test gave a 2-cm. area of erythema in forty-eight hours. The temperature gradually became normal. The patient was discharged three months after admission.

Final admission (six months later). In the interval he was taking digitalis, ferrous sulfate and components of the vitamin B complex. He felt better temporarily, and the spleen decreased in size, but later the weakness and malaise increased and he had an irregular fever. Two months previous to this admission he had an attack of left-upper-quadrant pain lasting for two days. One month later the left-upper-quadrant pain came on sharply and persisted. It was made worse by respiration, by lying on the left side and on motion and palpation of the left upper quadrant. The left shoulder and right knee were occasionally painful but not red, hot or swollen. Three weeks previous to admission he stopped the digitalis, and this did not result in increased dyspnea, cyanosis or edema. However, anorexia, malaise and fatigue became prominent symptoms, along with dry mouth, constipation and drowsiness. The urine was consistently dark.

Physical examination revealed a wasted lethargic man with fetid breath. There were numerous petechiae over the forearms, abdomen and thighs. The heart was not enlarged; there were harsh systolic murmurs at the apex and base and a high-pitched diastolic murmur in the aortic area along the left sternal border transmitted over the upper anterior portion of the chest. The aortic second sound was diminished. There were slight dullness and bronchial breathing over the left upper chest. The spleen was tender and greatly enlarged, reaching almost to the pelvis. The liver was 2 cm. below the rib margin and not tender. There was no dependent edema.

The temperature was 98.6°F., and the pulse 84 and regular. The blood pressure was 110 systolic, 60 diastolic.

The white-cell count was 4000, with 86 per cent neutrophils. The serum nonprotein nitrogen was 122 mg. per 100 cc., and the carbon dioxide 21.4 milliequiv. per liter. The urine repeatedly showed gross hematuria and albuminuria and a specific gravity ranging from 1.008 to 1.010. A chest film showed collapse of the left upper lobe as before, but there was complete disappearance of the pleural effusion. An electrocardiogram showed a partial auriculoventricular and intraventricular block. Blood cultures were negative.

The patient continued to have severe pain in the left shoulder and left upper quadrant, and he ate and drank very little. He was given fluids parenterally but no penicillin. The temperature and respiratory rate remained normal, whereas the pulse varied between 80 and 90. The nonprotein nitrogen rose progressively to 155 mg. per 100 cc., and the carbon dioxide fell to 16.6 milliequiv. per liter. He became disoriented and stuporous, and the skin petechiae increased in number. Finally one month after admission, the temperature, pulse and respirations increased to 100.5, 115 and 24 respectively, and he died the following morning, fourteen months after the onset of the illness.

Differential Diagnosis

Dr. Conger Williams: In summary this patient was a fifty-eight-year-old man who died of a wasting febrile disease, approximately fourteen months after the onset of the illness. The outstanding features were splenomegaly, only slight liver enlargement, which developed toward the end of the disease,

numerous petechiae, a persistent leukopenia and hematuria. On thinking over this very complicated problem, I believe that the possible diagnoses might be grouped under three headings. The first possibility is infection, the second, neoplasia, and the third, connective-tissue disease, such as periarteritis nodosa or lupus erythematosus.

Under the heading of infection, subacute bacterial endocarditis is the best possibility. This patient had definite heart disease, with systolic and diastolic murmurs, a persistent elevation of temperature, petechiae and successive episodes of left-upper-quadrant pain, suggesting recurrent emboli to the spleen. Another feature that fits with the diagnosis of subacute bacterial endocarditis is that of hematuria. However, I believe that macroscopic hematuria occurring so consistently during the course of subacute bacterial endocarditis is unusual. I also thought that the number of petechiae in this case was unusual. Ordinarily in subacute bacterial endocarditis, occasional petechiae are seen; when they occur in large numbers the more acute bloodstream infections or blood dyscrasias must be considered in the differential diagnosis. Another point in support of the diagnosis of subacute bacterial endocarditis was the development of the diastolic murmur along the left sternal border. Erosion of the aortic valve when it is the seat of a vegetative growth often produces such a murmur in the course of the disease. However, there is one point much against the diagnosis — the report that thirty-one blood cultures were negative. It is true that occasional cases of subacute bacterial endocarditis are seen in which a great many cultures are negative, possibly because an unusual organism, which is difficult to grow, happens to be the infecting agent. I think in this case thirty-one negative cultures are a strong argument against the diagnosis. Also, but less positively, against the diagnosis of subacute bacterial endocarditis is the lack of response to penicillin. This patient was given as much as 10,000,000 units a day over a period of one month. This does not rule out subacute bacterial endocarditis, but it does incline one a little bit against the diagnosis, especially in the absence of positive cultures.

No other diagnosis need be considered seriously under the heading of infections. Tuberculosis is a possibility in view of the long history of fluctuating temperature and the splenic enlargement and possibly the urinary findings. There was also a positive tuberculin test. However, I believed that the diagnosis of tuberculosis was very unlikely.

I think it might be a good plan to look at the x-ray films at this point.

Dr. Stanley M. Wyman: The films show that the heart is enlarged without any particularly characteristic configuration. The collapse of the left upper lobe is seen at the left apex, but the outline is imperfectly visualized in the lateral view. The film taken to show the bronchi is not satisfactory. There seems to be no definite obstruction in the bronchus itself. There is some calcification suggesting that the process is very old. The lung fields otherwise are clear. The film taken three weeks after this first film shows a considerable amount of fluid in the right side of the chest and to a lesser extent in the left. There is hazy density throughout the medial portions of the lung field spreading out from the hili. This cleared completely as is seen on the film taken several months later.

A pyelogram was done. The kidney shadows are of normal contour and size and show no evidence of calcification. The enlarged spleen is very easily seen lying almost at the level of the iliac crest. The dye was excreted in poor concentration by both kidneys after considerable delay, but the outline of the urinary passages is not sufficiently satisfactory to detect any but the grossest disease. I can see no definite abnormality. There is certainly nothing to suggest an active tuberculous lesion in the lung.

Dr. Williams: What about malignant tumors? Lymphoma is always a possibility when one is dealing with widespread systemic disease of this kind, and certainly it is capable of producing a persistent rise in temperature over a period of many months. Another thing that suggests the possibility is the fact that the leukopenia was rather marked and persistent. In lymphoma it is possible to have invasion of the bone marrow, with persistent leukopenia. Leukopenia, of course, is often the rule in subacute bacterial endocarditis, but it seems to me that the white-cell count was quite low, going as low as 3000 and even lower at times. Other points that suggest the possibility of lymphoma are the very persistent hematuria and albuminuria, indicating involvement of the renal tissues by a malignant process. As I said before, it is possible for the embolic phenomena in subacute bacterial endocarditis to produce this picture, but the amount and persistence of hematuria were a little bit unusual for that.

If one makes a diagnosis of malignant tumor, some of the clinical findings must be explained by assuming the presence of other disease. It seemed to me fairly definite that this patient had congestive heart failure at one time. This might be explained on the basis of long-standing aortic stenosis. Active rheumatic fever is another possibility, especially if the valvular lesions were the result of previous rheumatic infections. Recurrence of rheumatic fever is not uncommon during the course of subacute bacterial endocarditis. The possibility of myocardial involvement with a tumor process is remote. Mention was made at one point of the electrocardiographic finding of partial heart block and intraventricular block. Partial heart block is consistent with active rheumatic infection but also consistent with many other destructive lesions in the heart, as well as with coronary disease.

Metastatic carcinoma is a possibility, but I cannot imagine where the primary site would have been.

Another diagnosis to be considered is one of the "group" diseases. The possibility of periarteritis nodosa might explain the hematuria and albuminuria. The patient had a course of sulfadiazine earlier in the disease. It is well known that periarteritis nodosa may occur as a sensitivity reaction to sulfonamides, but that again is very remote. The possibility of lupus erythematosus always comes up but can hardly merit serious consideration here. I am left with two possibilities to explain the symptoms: rheumatic heart disease, with subacute bacterial endocarditis, and rheumatic heart disease with lymphoma. The thing that makes it difficult to accept subacute bacterial endocarditis is the large number of negative blood cultures, although almost everything in the history and findings suggests the diagnosis. I am inclined to accept the diagnosis of lymphoma.

Dr. Benjamin Castleman: How do you account for the change in the murmur on a straight rheumatic basis?

Dr. Williams: If the patient had active rheumatic infection he might well have had changing murmurs, especially if the infection were present over a long period. Also, a diastolic murmur could have been present before but might not have been heard.

Dr. Edward F. Bland: This case puzzled us for fourteen months. We went through the same line of reasoning. The fact that we were willing to treat the patient with 10,000,000 units of penicillin intramuscularly per day is an indication that we believed strongly in the diagnosis of subacute bacterial endocarditis.* The statement in the record that he had thirty-one negative blood cultures is a modest one, because he actually had a good many more. During the second admission the whole problem was one of uremia. He was totally afebrile, and the pulse was quiet. Further blood cultures up to the time of death were negative. Actually, he died in uremia, without fever or evidence of sepsis. The hematuria continued to the end. The systolic murmur dated back many years. He had no definite rheumatic fever, and because the physical signs were those of aortic stenosis, presumably since youth, we thought of the possibility of a calcified bicuspid valve.

Dr. Williams: Is it not unusual for a murmur heard twenty-five years previously to be based on a bicuspid valve? Of course another murmur, a functional murmur, may have been heard twenty-five years before.

Dr. Walter Bauer: I saw many such cases in the service.

Dr. Williams: I believe that the murmurs are heard as they become more calcified in later years.

*This large dosage of penicillin was made possible through the courtesy of the Lederle Laboratories, New York City.

Dr. Bland: When we see frank aortic stenosis in patients under the age of twenty, we believe that a considerable number have a bicuspid valve secondarily scarred by rheumatic fever.

Dr. Bauer: I thought that the diagnosis was subacute bacterial endocarditis. However, I did suggest the possibility of histoplasmosis or toxoplasmosis but not seriously.

Clinical Diagnosis

Subacute bacterial endocarditis.

Dr. Williams's Diagnoses

Rheumatic heart disease, with aortic stenosis and regurgitation.
Lymphoma.

Anatomical Diagnoses

Subacute bacterial endocarditis.
Congenital bicuspid aortic valve.
Bronchopneumonia.
Subacute glomerulonephritis.
Healed pulmonary tuberculosis.
Infarcts of the spleen, multiple.

Pathological Discussion

Dr. Tracy B. Mallory: We have a photograph of the heart, which was slightly enlarged and showed a bicuspid aortic valve (Fig. 1). The valve flaps were covered with warty vegetations, and at one point there was a perforation through the cusp. A blood culture taken at the time of post-mortem examination was negative. However, in cultures made directly from the vegetations, alpha-hemolytic streptococcus grew out. When the organism was tested for penicillin sensitivity it was found to be extremely resistant, being inhibited only at 5 units per cubic centimeter, the highest dosage in which we tested it. The other point of major interest was the kidneys, which weighed 250 gm., were small for a man and showed scattered petechiae over the surface. Microscopical sections did not particularly suggest the focal or embolic type of nephritis usually seen in subacute bacterial endocarditis. I would classify the lesion as subacute or early chronic diffuse glomerulonephritis, which is also sometimes seen with bacterial endocarditis.

Microscopical sections of the heart valves showed extensive calcification of the vegetations, but foci of activity were still present. One rather unusual feature that I cannot remember ever having seen before was a small island of cartilage formation in one of the cusps. One sometimes sees metaplastic bone formation, but I do not happen to have seen metaplastic cartilage before in a heart valve.

The spleen weighed 650 gm. and showed three separate old infarcts. There were widespread petechiae throughout the body, skin and mucous membranes. There were a number of spots of fibrosis and one spot of fresh local infarction in the myocardium itself — unquestionably the result of very

small emboli in the coronary system. At the time of death the patient also had an extensive bronchopneumonia.

DR. BAUER: At the time of autopsy was the lung consolidated?

DR. MALLORY: There was an old emphysema and fibrosis but no evidence of active tuberculosis.

DR. BAUER: Was there any evidence of bronchial disease?

DR. MALLORY: No.

DR. BLAND: This case illustrates one of the first patients that we have had the courage to treat so vigorously on suspicion alone. In looking back, we were right, but perhaps we did not go far enough.

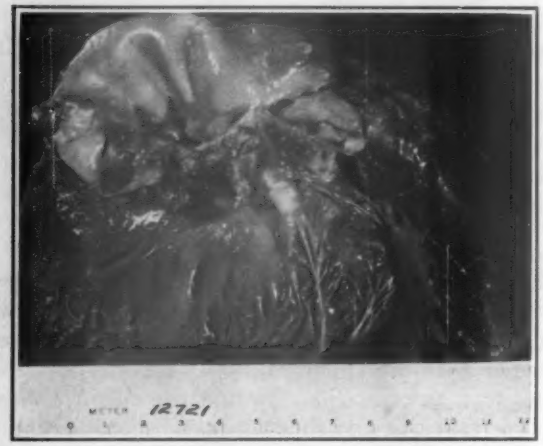

FIGURE 1.

The case illustrates the fact that older people with bacterial endocarditis are apt to run a milder course and that the disease is consequently more difficult to recognize. Of course, it is easy now, but in retrospect we thought that we had controlled the disease since the patient was better when he went home after the first admission. I would like to ask Dr. Bauer if he thinks we should have been even more courageous and given streptomycin. We were afraid of sulfadiazine because of the renal situation and because he was bordering on uremia even at the first admission.

DR. BAUER: In retrospect, yes. At the time I saw the patient I was opposed to continuing treatment because I did not believe that penicillin would be effective. I had no right to make that statement because we did not know the causative organism or its penicillin sensitivity.

CASE 34112

PRESENTATION OF CASE

First admission. An eighty-nine-year-old woman was first admitted to the hospital with a five-day history of constipation and gradually increasing distention.

The patient had been perfectly well until admission and had normal bowel habits. There was no history of melena.

Physical examination showed a well preserved woman in no discomfort. There was marked kyphoscoliosis to the right. The heart sounds were snapping, and there was a soft apical systolic murmur. The abdomen was distended, tense and tympanitic, with rushed normal-pitched peristalsis in the left lower quadrant. On rectal examination at the end of the finger was an irregular mass almost encircling the rectum, which felt as though it lay outside the mucosa. This was nontender, and there was no blood on the examining finger.

The temperature, pulse and respirations were normal.

A temporary cecostomy was done the next day. A week later a sigmoidoscopy was done, which showed no intrinsic tumor tissue, and a permanent double-barreled colostomy was made. At this operation the surgeon noted an area of diverticulosis of the sigmoid about 10 cm. long at the end of which was a tight constriction. There was no involvement of the peritoneum by tumor. The patient was discharged two months later.

Second admission (five years later). In the interval she had been in fairly good health. She had severe rectal tenesmus occurring in spasms several times a day, with the passage of moderate amounts of mucus and blood at times during the past year. A year before readmission she passed a mass the size and shape of a duck's egg. This was made up of inspissated mucus with no blood. Six months later she entered another hospital complaining of chills, fever and low abdominal tenderness, but this cleared up with sulfadiazine. At that time and on numerous other occasions, rectal examination showed a narrowing of the rectum, beginning 10 cm. from the anus, with a large mass about it and filling the pelvis. Three days before readmission she began to have severe chills and fever and lower abdominal pain. On the day of admission there was abdominal distention and passage of nothing by colostomy.

Physical examination revealed slight tenderness in the lower abdomen and normal-sounding peristalsis. The blood pressure was 100 systolic, 60 diastolic. A rectal examination was reported as follows: "At one finger's length inside the anus is a large, hard, tender, slightly movable mass with a central small lumen that admits the tip of the finger. There is blood on the rectal glove."

The white-cell count was 30,000, with 90 per cent neutrophils. The hemoglobin was 9.7 gm., and the serum nonprotein nitrogen was 42 mg. per 100 cc. The urine contained albumin and many pus cells.

A plain film of the abdomen showed numerous dilated loops of small and large bowel, with no gas in the distal sigmoid.

A colostomy irrigation resulted in the passage of much gas.

The patient was given penicillin and streptomycin but continued to have a low-grade fever, the temperature ranging from 99 to 101°F., with occasional elevations to as high as 103°F. The pulse varied from 80 to 100, and the respirations from 20 to 30. Repeated laboratory studies continued to show leukocytosis, albuminuria and pyuria. There was a rectal discharge, and irrigations yielded dark-green mucoid material. Finally she had great urinary frequency and was placed on constant bladder drainage. She died eight weeks after admission.

Differential Diagnosis

Dr. Joseph A. Holmes: Although it is fairly evident that this patient's two admissions were related, and it may be shown that there was only one lesion responsible for the illness at both admissions, I shall discuss each admission separately.

We have a very short and meager history of the illness prior to the first admission. Two pertinent statements were made, however — that she had been well, with normal bowel movements, and that there was no history of melena. A five-day history of constipation and gradually increasing distention leads one immediately to the assumption that there was probably frank obstruction, primarily in the large bowel, especially in the absence of any note regarding cramps, pain or vomiting.

On physical examination the findings were quite remarkable for a woman of eighty-nine years. Small-bowel obstruction appears to have been ruled out by the presence of normal-pitched peristalsis and by the absence of elevation of pulse, temperature and respirations. On rectal examination a mass was noted, although the examiner appears to be quite definite in the statement that the mass lay outside the rectal mucosa. No blood was noted on the examining finger.

We have no laboratory data on the first admission, nor is any statement made of a plain film of the abdomen. I doubt that such information would be of any assistance other than to confirm our impression that she had an acute obstruction. There is no mention of the passage of gas by rectum, so I shall assume that there was none and that there was sufficient evidence of large-bowel obstruction so that a cecostomy was done the following day. The decompression apparently relieved her sufficiently so that a week later the exploration of the abdomen could be carried out. At operation an area of diverticulosis of the sigmoid was noted, and at the lower end of this area a tight constriction was found. There was no involvement of the peritoneum or of the perirectal tissue by tumor, and no tissue was removed for biopsy.

I believe that the discussion of such cases as this at these conferences has emphasized the frequency with which carcinoma is associated with diverticulitis of the sigmoid colon. No intrinsic tumor tissue was noted on sigmoidoscopic examination, and I am totally in agreement with the operator that in such circumstances one must assume that the entire lesion is on the basis of diverticulosis, with an area of diverticulitis at the lower end. It is probably next to impossible at operation to distinguish frank cancer associated with diverticulitis from a cicatrizing inflammatory process. I am emphasizing this because of the importance that is attached to the sigmoidoscopic examination as a preoperative procedure.

There are numerous factors involved in this case, and it is for those managing the case at the time to make the decision. Certainly the patient had lived beyond the average life span, and we know little enough about her nutrition and general condition to encourage a more radical procedure than was carried out. A permanent double-barreled colostomy was done, and she was discharged two months later.

Turning now to the second admission, five years later, we find that she had been well over this period except that she had had severe rectal tenesmus and had passed moderate amounts of mucus and blood at various times during the past year. It is obvious that there was a progressive change in the local lesion in the rectum. There was definite involvement of the mucosa, and the lumen had become smaller. There was also evidence of an inflammatory process in that she was running a low-grade fever, with occasional temperature elevations to 103°F. and an elevation in the white-cell count. A fairly marked anemia was present.

Much of the evidence presented in this case leads one to believe that the lesion noted at the original operation, which persisted to death, might possibly have been that of an annular carcinoma. However, from the various studies of untreated cases of carcinoma of the colon, the life expectancy in these cases at best is not over twenty months. In the cases reported by Nathanson and Welch* the expectancy was only fourteen months. It is necessary, then, to consider other possibilities.

Tuberculosis of the rectum is such a rare disease that I feel justified in dismissing it, particularly on the basis of the findings at the original laparotomy.

Other granulomatous lesions should be considered. Actinomycosis is a very rare disease, and such a lesion present for five years, I believe, would have caused fistulas either above or below.

There remain then few other possibilities. Malignant melanoma of the bowel, although rare, occurs frequently enough to be seriously considered in any age group. I wanted to make that diagnosis in this case, believing that the mention of the dark-green material returned with the rectal irrigations might be a clue to the nature of the lesion. This sort of material is not typical of melanoma. Again, a melanoma of the rectum would have been detected either

*Nathanson, I. T., and Welch, C. E. Life expectancy and incidence of malignant disease. III. Carcinoma of gastro-intestinal tract. *Am. J. Cancer* **31**:457-466, 1937.

on sigmoidoscopic examination or by the appearance of the bowel at the time of operation. Also, a melanoma is usually a rapidly growing lesion and if present for five years should, I believe, have become quite distinctly larger locally, with evidence of wide spread to other tissues such as the liver. No mention is made of an enlarged liver. On a similar basis, I shall exclude lymphoma of the bowel, for I believe that the lesion existed too long to have confined itself to the original locale.

This leaves me but one choice — an inflammatory process, which could well have occurred on the basis of diverticulitis alone or on the basis of diverticulitis and the presence of a foreign body that had become lodged in the area of constriction, with the subsequent development of a pelvic abscess, which gradually increased in size. We know that she had diverticulosis at the time of the first admission, and we know that diverticulitis can produce the narrowing described. I believe that the duration of the lesion over a five-year period is in favor of that diagnosis, as is the description of the terminal illness. The increased size of the local lesion can be accounted for by the formation of an abscess about it, even though the bowel had been nonfunctioning. I believe that the evidence points more toward this, with the spread of the infection eventually to involve the small intestine, causing partial obstruction to the small bowel. My diagnosis, then, remains as diverticulitis as the primary disease, with terminal abscess formation and small-bowel obstruction.

Dr. Ernest M. Daland: I first saw this patient at her home in the middle of the night. I brought her to the hospital and did a cecostomy under novocain at once. No x-ray studies were made before the second operation. The point of obstruction was obvious — high in the rectum. No tissue for biopsy could be obtained on proctoscopic examination. Only the ampulla could be inspected by the proctoscope, since obstruction was complete.

Before the exploratory operation my diagnosis was carcinoma. Afterward, because of the area of diverticulosis visualized, I believed that there was a chance that the entire process was diverticulitis. I raised the question of cancer. I told the family that I could not tell which it was but that time alone would tell.

As each of the five years passed until the next hospital admission, with very little change in the examinations, it seemed probable that the disease was diverticulitis and not cancer. During the final illness the presence of pus in the urine, the bladder irritability, the fever and the high white-cell count made me believe that the patient had a pelvic abscess from the diverticulitis and that she probably had a bladder fistula. No attempt was made to prove this, for it was believed that the treatment already instituted would not be changed.

Clinical Diagnosis

Diverticulitis of sigmoid, with pelvic abscess and fistula into bladder.

Dr. Holmes's Diagnosis

Diverticulitis of sigmoid, with pelvic abscess.

Anatomical Diagnoses

Adenocarcinoma of rectosigmoid (Grade II), with secondary abscess formation and extension into pelvis and uterus.
Pyometrium.
Pyelonephritis, acute and chronic, left.
Diverticulosis of sigmoid.

Pathological Discussion

Dr. Benjamin Castleman: At autopsy most of the pelvis was replaced by necrotic, friable, pale-yellow tumor, which had broken down in many areas to form green purulent abscesses. The tumor originated in the rectosigmoid and was about 8 cm. long and completely annular. It had infiltrated both sides of the pelvis and extended into the uterus at the internal os to produce a pyometrium. The left ureter was surrounded by tumor in the pelvis and led to a mild pyelonephritis. Above the tumor the sigmoid contained many diverticula, but there was no evidence of infection within or around them.

The rectosigmoid tumor was a well differentiated adenocarcinoma, and I believe it might well have been present at the first operation five years before death. Tumors in elderly persons are very apt to grow slowly, invade only locally and not metastasize. Although one cannot absolutely rule out the development of the cancer on the basis of a pre-existing diverticulitis, I am more in favor of its having been present at the original admission.

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THE BOSTON HEALTH LEAGUE

Until 1948 the Boston Health League had not published a report since 1940. The current report, therefore, covers considerable ground, accounting for the League's activities both during the war and in the post-war period, from 1941 to 1947.

In March, 1941, the League formed the subcommittee on health of the Committee on Public Safety to co-ordinate the city's health activities with the general defense plan. After Pearl Harbor the Health League and the Hospital Council of Boston participated actively in the Health Services Division of the Committee on Public Safety, the executive secretary of the League and the Hospital Council acting as secretary of the Division.

A committee of the League in 1940 reviewed the mental-hygiene situation in Boston agencies to bring up to date a decade's progress since the last previous survey. In 1943 a joint committee of the Massachusetts Society for Mental Hygiene and the Health League was formed to consider mental-hygiene problems aggravated by the war situation.

In 1941 a committee was appointed to reappraise nutrition work in Boston. In 1945, at the request of the First Service Command and the First Naval District a committee on venereal disease was organized. As a result of the activities of this committee the reporting of cases of venereal disease showed a marked improvement.

Many of the regular activities of the League were maintained during the war years. It continued its work on the Group Budget Committee on Health of the Greater Boston Community Fund. It cooperated actively with the School Committee of Boston in the establishment of a unified school lunch program, under the administration of a qualified director.

In 1943 the Boston Council of Social Agencies was reorganized and became the Greater Boston Community Council. In the following spring the Boston Health League joined it, maintaining its identity, however, within the Health and Hospital Division. This has made it inevitable that metropolitan problems should come under the scrutiny of the League, although its concern remains primarily with municipal Boston.

A review of the structure and the activities of the Health League accordingly seemed indicated, and this was made in 1947. As a result of this study it seemed wise that the structure of the League should be truly representative, with a membership composed of all important agencies, voluntary and official, working in the health field, and with integration with the Hospital and Nursing Council and the Medical Social Work group.

At the annual meeting in March, 1947, member agencies agreed that the League should stand ready to point out needs in the health field; to define, allowing for flexibility, the fields of responsibility of official and voluntary agencies; to carry out, in cooperation with the Research Bureau of the Community Council studies to develop new standards and technics and to evaluate present programs.

BAGASSE DISEASE OF THE LUNGS

An industrial disease, formerly rare but showing promise of becoming more prevalent, has recently been described by LeMone, Scott, Moore and Koven.* This is bagassosis, a condition that results from exposure to the dust of bagasse, or sugar cane after it has been crushed and the juice extracted. This by-product of the sugar industry is finding increasing use in the manufacture of acoustical and thermal insulating building materials and in the production of refractory brick.

The disease has been reported in Cuba, England, Louisiana and Missouri, where these products are made, and will probably spread to other areas as the industrial potentialities of bagasse are exploited.

Bagasse dust consists of pith particles with a small quantity of bundles and rind fibers, numerous assorted bacteria and millions of fungous spores. Although its ash contains some silica, the amount is thought to be insignificant. After an average of about two months' exposure, the susceptible person succumbs to an acute febrile illness with extreme dyspnea, a persistent cough, scanty mucoid sputum and profound weakness. A leukocytosis, with a shift to the left and eosinophilia, is present. Treatment is symptomatic, with oxygen as needed for acute dyspnea. Drugs and antibiotics appear valueless. The mortality is about 8.3 per cent, which, coupled with a morbidity of two months to over a year, makes it obvious that this is an industrial disease of a serious nature.

On x-ray examination, an extensive punctate pulmonary infiltration is found that may coalesce into pneumonic areas. The picture is not characteristic of the disease but is similar to other pneumoconioses. The pulmonary changes are reversible as recovery occurs and have cleared in most cases without residual effects, thus differing from most pneumoconioses.

Pathologically, cellular debris is found in the alveoli and bronchioles, with fibroblastic reaction of the interstitial tissue. Within the area of reaction needle-like spicules of irregular foreign material similar to bagasse are observed. The disease has been interpreted as an organic pneumoconiosis of which the exact etiology is unknown, exposure to bagasse dust initiating the disease pattern. The possible role of contaminating fungi, bacteria and viruses has been considered as well as an allergic response to them and to the constituents of bagasse itself. No specific organisms have been found.

Prevention depends upon a dust-free environment such as may be obtained by a change to a wet method of collecting and opening the bales of bagasse.

*LeMone, D. V., Scott, W. G., Moore, S., and Koven, A. L. Bagasse disease of lungs. *Radiology* 5:556-567, 1947.

ANNABELLA McCRAE

Annabella McCrae, who died at the Massachusetts General Hospital on February 1, 1948, was born in Beauharnois, P. Q., in November, 1863. She graduated from the nursing school of the McLean Hospital in 1893, and two years later from the Training School for Nurses of the Massachusetts General Hospital. Here she became instructor of nursing art in 1902 and held the position until her retirement in 1934.

Miss McCrae can hardly be placed in the same category with Florence Nightingale or Clara Barton or Linda Richards. She was not in any similar sense a pioneer, nor was she in any sense in the public eye. And yet for thirty-three years, in a community that has long prided itself on its reputation for public service, she probably did more than any other single person to elevate and maintain the standards of nursing care.

During the period of her instructorship, 1953 graduates of the training school came under the influence of Annabella McCrae, and indifferent indeed was the girl who did not become thereby a better and a more useful nurse and woman. Miss McCrae had no patience with inferior performance or with an oblique attitude toward any problem. In her own mind and in her teaching, her loyalty to the medical profession was complete. Rigid in her standards of excellence, she was flexible in her acceptance of the changes that progress brings. She was willing and eager to learn from whoever had something to teach, that she might utilize the new knowledge in her own instruction.

She was the champion (often in disguise) of the frightened probationer, and, awesome as she might

sometimes have seemed, moving in grim majesty through the brick corridors of her hospital, those who knew her, knew her as a friend. She has left a deep imprint on the teaching of the art of nursing. That imprint bears the mark of unselfish devotion to a high calling, of practical idealism and of unflinching integrity.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DODD — Isaac S. F. Dodd, M.D., of Pittsfield, died on January 29. He was in his eightieth year.

Dr. Dodd received his degree from New York University Medical College in 1890. He was a former president of the Berkshire District Medical Society, a former vice-president of the Massachusetts Medical Society and a former supervising censor. He was formerly chief of staff, House of Mercy Hospital, and was a fellow of the American College of Surgeons and American Medical Association.

His widow, a son and a daughter survive.

HOBERMAN — Samuel Hoberman, M.D., of Malden, died on February 18. He was in his sixty-sixth year.

Dr. Hoberman received his degree from George Washington University School of Medicine in 1907. He was physician-in-charge at the Malden Hospital for twenty-five years and was a fellow of the American Medical Association.

His widow, three daughters and a son survive.

O'BRIEN — Edward J. O'Brien, M.D., of Boston, died on February 16. He was in his sixty-first year.

Dr. O'Brien received his degree from Tufts College Medical School in 1912. He was surgeon-in-chief at the Cambridge City Hospital, consultant to Metropolitan State Hospital, Waltham, Boston State Hospital, Somerville, Choate Memorial Hospital, Woburn, and Winchester Hospital and urologist at St. Elizabeth's Hospital, Brighton, for nearly thirty years. He was a member of the New England Obstetrical and Gynecological Society and the American Urological Association and a fellow of the American College of Surgeons and the American Medical Association.

Four sons and a daughter survive.

OSBORNE — Carver H. Osborne, M.D., of Brookline, died on January 3. He was in his fifty-first year.

Dr. Osborne received his degree from Boston University School of Medicine in 1921. He was formerly a member of the staff of Truesdale Hospital in Fall River. He was a fellow of the American Medical Association.

His widow and a sister survive.

REIS — Frederick Reis, M.D., of Jamaica Plain, died on February 4. He was in his seventy-second year.

Dr. Reis received his degree from Tufts College Medical School in 1903. He was professor of physiology and biochemistry at Tufts College Medical School. He was a member of the Massachusetts Medico-Legal Society and the American Chemical Society.

His widow survives.

SMITH — Frederick G. Smith, M.D., of Somerville, died on January 9. He was in his eighty-first year.

Dr. Smith received his degree from University of Michigan Medical School in 1893. He was a member of the staff of Somerville Hospital, where he was formerly chairman of the medical board. He was a former councilor of the Massachusetts Medical Society and was a fellow of the American Medical Association.

His widow, a daughter and a son survive.

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Daniel N. Beers, *Secretary*
74 North Street, Pittsfield

BRISTOL NORTH DISTRICT

BARNES, WILLIAM E., 1 Prospect Street, Taunton.
Tufts College Medical School, 1945.

COREN, SIMON, 134 Pleasant Street, Attleboro.
Middlesex University School of Medicine, 1940. Sponsor: Isadore Altman, 70 Church Street, North Attleboro.

LOEB, ELSIE K., 142 North Washington Street, North Attleboro.
University of Munich, 1936. Sponsor: James H. Brewster, 178 South Main Street, Attleboro.

TERRANOVA, ANTHONY J., 225 South Main Street, Attleboro.
Middlesex University School of Medicine, 1939. Sponsor: Frederick V. Murphy, 79 Bank Street, Attleboro.

VELON, BRUCE P., 137 Broadway, Taunton.
Middlesex University School of Medicine, 1937. Sponsor: Myer Bloom, 20 Cedar Street, Taunton.

William E. Dawson, *Secretary*
58 Winthrop Street, Taunton

BRISTOL SOUTH DISTRICT

JENNEY, WILLIAM L., 65 Ryan Street, New Bedford.
Yale University School of Medicine, 1945.

MACKLER, EDWARD D., 359 Pleasant Street, New Bedford.
Tufts College Medical School, 1945.

MARTENS, THEODORE G., 218 Calvin Street, Fall River.
University of Rochester School of Medicine, 1943.

NEVES, EDMUND F., 78 Langley Street, Fall River.
Jefferson Medical College of Philadelphia, 1942.

PEREIRA, MANUEL C., 329 Foley Avenue, Somerset Center.
University of Coimbra, Faculty of Medicine, Portugal, 1920. Sponsor: Warren G. Atwood, 151 Rock Street, Fall River.

POWERS, HARRY T., 633 Robeson Street, Fall River.
Cornell University Medical College, 1943.

RAPPAPORT, DAVID, Circuit Avenue, Oak Bluffs.
Middlesex University School of Medicine, 1942. Sponsor: Robert W. Nevin, Edgartown.

SULLIVAN, THOMAS H., 78 Grant Street, Fall River.
Middlesex University School of Medicine, 1930. Sponsor: Hilary F. White, 95 Cottage Street, Fall River.

WITMER, DONALD S., 169 Belmont Street, Fall River.
College of Physicians and Surgeons, Boston, 1939. Sponsor: H. Leonard Bolen, 1524 South Main Street, Fall River.

James E. Fell, *Secretary*
181 Purchase Street, Fall River

ESSEX NORTH DISTRICT

BLOTNER, CARL, 248 Broadway, Lawrence.
St. Louis University School of Medicine, 1933.

KAPLAN, LOUIS S., Beach Road, Salisbury.
Middlesex University School of Medicine, 1933. Sponsor: Clarence R. Hines, 39 Market Street, Amesbury.

LEE, CHARLES F., 93 Elm Street, North Andover.
Middlesex University School of Medicine, 1936. Sponsor: John J. Hartigan, 57 Jackson Street, Lawrence.

MILLER, NATHANIEL B., 222 South Main Street, Haverhill.
Middlesex University School of Medicine, 1938. Sponsor: Paul Nettle, 282 South Main Street, Haverhill.

WHOLEY, JOHN J., 5 Birch Street, Lawrence.
Middlesex University School of Medicine, 1942. Sponsor: Thomas V. Uniac, 46 Amesbury Street, Lawrence.

WOODMAN, ERNEST L., JR., Warwick Street, Lawrence.
Tufts College Medical School, 1939.

ZAWISLAK, JOSEPH J., 38 Avon Street, Lawrence.
Middlesex University School of Medicine, 1936. Sponsor: John J. Hartigan, 57 Jackson Street, Lawrence.

Harold R. Kurth, *Secretary*
57 Jackson Street, Lawrence

ESSEX SOUTH DISTRICT

BARKAN, DONALD B., 119 Lynn Shore Drive, Lynn.
Boston University School of Medicine, 1945.

BELL, W. RANDAL, 36 Locust Street, Marblehead.
Yale University School of Medicine, 1941.

BELOCK, JOHN E., 41 Cogswell Avenue, Beverly.
University of Vermont College of Medicine, 1944.

BROWN, C. BRUCE, 92 Main Street, Rockport.
University of Toronto Faculty of Medicine, 1931.

DAVIS, STILMAN G., JR., 38 Granite Street, Nashua, New Hampshire.
University of Vermont College of Medicine, 1943.

GEWIN, EDWIN E., 80 Middle Street, Gloucester.
University of Tennessee College of Medicine, 1929.

MICHAUD, RAYMOND R., 10 Central Street, Beverly.
Tufts College Medical School, 1945.

ROSENGARD, DAVID E., 43 Eastern Avenue, Lynn.
Tufts College Medical School, 1945.

SHEA, DANIEL J., JR., Beverly Hospital, Beverly.
Boston University School of Medicine, 1945.

Henry D. Stebbins, *Secretary*
342 Essex Street, Salem

HAMPDEN DISTRICT

BILSKI, THEODORE D., 12 Pleasant Street, Westfield.
University of Halle, Germany, 1922. Sponsor: Archibald J. Douglas, 69 Broad Street, Westfield.

BLANEY, CHARLES L., 435 Roosevelt Avenue, Springfield.
Cornell University Medical College, 1940.

BRONSON, BENJAMIN, 18 McKinley Terrace, Westfield.
Middlesex University School of Medicine, 1925. Sponsor: Edward S. Smith, Westfield.

BURKHARDT, HENRY, 1 Brockway Lane, South Hadley.
Wayne University College of Medicine, 1943.

CALLAHAN, CHARLES L., 74 Berkshire Street, Indian Orchard.
Georgetown University School of Medicine, 1938.

CORWIN, HARRY J., 78 South Main Street, East Longmeadow.
Middlesex University School of Medicine, 1938. Sponsor: George L. Steele, 20 Maple Street, Springfield.

DIXON, STANLEY R., 698 Alden Street, Springfield.
Missouri College of Medicine and Surgery, 1927. Sponsor: Arthur F. G. Edgelow, 76 Maple Street, Springfield.

DORFMAN, WILLIAM A., 31 Rupert Street, Springfield.
Middlesex University School of Medicine, 1941. Sponsor: Arthur J. Horrigan, 20 Stratford Terrace, Springfield.

GOODWIN, ARTHUR H., 300 Main Street, Wilbraham.
Tufts College Medical School, 1941.

HAENTZSCHEL, LESTER E., 43 Benedict Terrace, Longmeadow.
Washington University School of Medicine, 1937.

HALTON, GERALD J., 1454 Northampton Street, Holyoke.
Cornell University Medical College, 1944.

HAMBLIN, WILLIAM N., 8 Riverside Drive, Westfield.
Syracuse University College of Medicine, 1942.

HURLEY, FRANK E., 107 Harvard Street, Springfield.
Tufts College Medical School, 1943.

MOORE, FREDERICK T., 74 Warren Street, West Springfield.
Tufts College Medical School, 1941.

NEWMAN, WALTER, 115 State Street, Springfield.
University of Graz, Austria, 1923. Sponsor: Max Millman, 111 Maple Street, Springfield.

SOTIRION, GEORGE A., 353 Maple Street, Springfield.
Duke University School of Medicine, 1940.

TAGGART, WILLIAM G., 11 King Street, Westfield.
Jefferson Medical College of Philadelphia, 1933.

TAUBER, JOSEPH, 820 State Street, Springfield.
University of Vienna, 1921. Sponsor: Alfred Hollander, 458 Bridge Street, Springfield.

George C. Steele, *Secretary*
39 Upper Church Street, West Springfield

HAMPSHIRE DISTRICT

ALBERTSON, MIRIAM A., 58 Paradise Road, Northampton.
University of Nebraska College of Medicine, 1926.

JENNISON, DAVID B., 24 Ward Avenue, Northampton.
Harvard Medical School, 1938.

F. Mary P. Snook, *Secretary*
Worthington

MIDDLESEX EAST DISTRICT

HOLDEN, ROBERT B., 121 Florence Street, Melrose.
Harvard Medical School, 1943.

Roy W. Layton, *Secretary*
8 Porter Street, Melrose

MIDDLESEX NORTH DISTRICT

BARNES, WILLIAM L., Pleasant Street, Tewksbury.
Middlesex University School of Medicine, 1941. Sponsor: Mason D. Bryant, 9 Central Street, Lowell.

KALIKA, KARL, 598 Wilder Street, Lowell.
Midwest Medical College, 1934. Sponsor: Samuel A. Dibbins, 310 Merrimack Street, Lowell.

REPPUCCI, ANTHONY, 187 Nesmith Street, Lowell.
Middlesex University School of Medicine, 1942. Sponsor: Leo F. King, 310 Merrimack Street, Lowell.

Brendan D. Leahey, *Secretary*
9 Central Street, Lowell

MIDDLESEX SOUTH DISTRICT

ANDERSON, ERNEST G., 91 Brookside Avenue, Belmont.
Friedrich-Wilhelm University of Berlin, 1924. Sponsor: H. Quimby Gallupe, 33 Linden Park Drive, Waltham.

BLACKLOW, DANIEL J., 330 Mt. Auburn Street, Cambridge.
Tufts College Medical School, 1944.

BLOTNICK, WILLIAM, 101 Forest Street, Medford.
Middlesex University School of Medicine, 1942. Sponsor: J. Laurence Golden, 333 Winthrop Street, Medford.

BONZEY, CHARLES M., JR., 6 Surrey Lane, Natick.
Boston University School of Medicine, 1944.

COSTIN, MAURICE E., 167 Union Avenue, Framingham.
Harvard Medical School, 1942.

CRANE, EMILY BROWNE TOWNSEND, 195 Marsh Street, Belmont.
Cornell University Medical College, 1945.

CRONIN, THOMAS P., JR., 6 Dartmouth Street, Somerville.
Columbia University College of Physicians and Surgeons, 1943.

GROGAN, RICHARD H., 158 Russell Avenue, Watertown.
Harvard Medical School, 1939.

HUTCHINS, GRETCHEN, 247 Chestnut Hill Avenue, Brighton.
Yale University School of Medicine, 1941.

INGERSOLL, ROBERT E., 14 Bradford Street, Belmont.
University of Rochester School of Medicine, 1939.

LOCKSHIN, ABRAHAM D., 514A Main Street, Medford.
Middlesex University School of Medicine, 1941. Sponsor: Michael C. Nash, 43 Forest Street, Medford.

MALONE, EDWARD H., 216 Varick Road, Waban.
Boston University School of Medicine, 1943.

MAYNARD, GUY B., JR., 32 Bishopsgate Road, Newton.
Cornell University Medical College, 1943.

MCMANAMA, JOHN C., 15 Church Street, Waltham.
Tufts College Medical School, 1941.

MERLIS, JEROME K., 58 Main Street, Framingham Centre.
University of Louisville School of Medicine, 1937.

MOLL, FREDERIC C., 247 Chestnut Hill Avenue, Brighton.
University of Rochester School of Medicine, 1940.

MURRAY, EDWARD S., 36 Cushing Avenue, Belmont.
State University of Iowa College of Medicine, 1938.

PAGLIUCA, GERALD F., 97 Dartmouth Street, Medford.
College of Physicians and Surgeons, Boston, 1934. Sponsor: John W. Gahan, 27 Washington Street, Medford.

PETERS, JAMES M., 14 Rice Street, Newton Center.
Tufts College Medical School, 1939.

RAMSAY, BEATTY H., 799 Concord Avenue, Cambridge.
University of Manitoba Faculty of Medicine, 1940.

ROCKWOOD, LAWRENCE, 79 Governors Avenue, Medford.
Boston University School of Medicine, 1943.

SCHLESSINGER, PAUL J. R., 16 Chatham Street, Cambridge.
Harvard Medical School, 1944.

SEELER, ALBERT O., 64 Royce Road, Newton Centre.
Harvard Medical School, 1938.

SELVERSTONE, BERTRAM, 142 Payson Road, Belmont.
Harvard Medical School, 1941.

SKORNIK, NATHAN H., 1516 Washington Street, West Newton.
Middlesex University School of Medicine, 1940. Sponsor: Stephen Rushmore, 95 Dudley Road, Newton Centre.

TAFT, EDGAR B., 21 Walker Street, Cambridge.
Yale University School of Medicine, 1942.

TALBOT, TIMOTHY R., JR., 113 Maplewood Street, Watertown.
University of Pennsylvania School of Medicine, 1941.

WARING, GEORGE W., JR., 1568 Commonwealth Avenue, Brighton.
Johns Hopkins University School of Medicine, 1943.

Alexander A. Levi, *Secretary*
481 Beacon Street, Boston

NORFOLK DISTRICT

ARMSTRONG, CATHERINE, 115 Wellesley Avenue, Wellesley.
University of Vermont College of Medicine, 1933.

ARNOT, ROBERT E., 201 St. Paul Street, Brookline.
Harvard Medical School, 1940.

BERMAN, SAMUEL S., 277 Warren Street, Roxbury.
Middlesex University School of Medicine, 1935. Sponsor: Edward S. Calderwood, 219 Warren Street, Roxbury.

BRADFORD, MARTIN L., 9 Goodrich Place, Sharon.
Boston University School of Medicine, 1942.

BRAGG, ERNEST A., JR., 82 Washington Street, Wellesley Hills.
Boston University School of Medicine, 1943.

BROOKS, OSCAR D., 125 Melville Avenue, Dorchester.
Middlesex University School of Medicine, 1930. Sponsor: Joseph H. Carey, 103 Melville Avenue, Dorchester.

CROWELL, DAVID P., Glezen Lane, Wayland.
Boston University School of Medicine, 1942.

ECHLOV, THEODORE G., 1682 Beacon Street, Brookline.
Middlesex University School of Medicine, 1940. Sponsor: William Dameshek, 192 Beacon Street, Boston.

GOTTLER, JACOB, 60 American Legion Highway, Dorchester.
Boston University School of Medicine, 1942.

GRAY, BASIL C., 7 Fuller Road, Wellesley Hills.
Syracuse University College of Medicine, 1937.

GREER, WILLIAM E. R., 41 Morton Street, Jamaica Plain.
Boston University School of Medicine, 1943.

HALPERN, WILLIAM, 40 Blake Road, Brookline.
University of Pennsylvania School of Medicine, 1937.

HERTZMARK, FREDERIC, 976 Blue Hill Avenue, Dorchester.
University of Buffalo School of Medicine, 1939.

HOCHSTADT, OTTO, 5 Vinal Street, Brookline.
University of Vienna, 1932. Sponsor: Humphrey L. McCarthy, 479 Beacon Street, Boston.

HUBBELL, JOHN P., JR., 605 Chestnut Hill Avenue, Brookline.
Harvard Medical School, 1943.

HURLEY, PAUL D., 37 Castleton Street, Jamaica Plain.
Tufts College Medical School, 1939.

KARLIN, HAROLD, 339 Tappan Street, Brookline.
Boston University School of Medicine, 1942.

KEINER, SAMUEL S., 1203 Beacon Street, Brookline.
Middlesex University School of Medicine, 1936. Sponsor: Jacob Applebaum, 371 Commonwealth Avenue, Boston.

LEARY, GERALD C., 48 Lake Shore Drive, Westwood.
Tufts College Medical School, 1941.

LICHTY, JOSEPH S., 40 Griggs Road, Brookline.
Harvard Medical School, 1933.

MCVAY, JOHN F., 11 Van Brunt Avenue, Dedham.
Tufts College Medical School, 1944.

MILLS, WALDO O., 67 Carlton Street, Brookline.
University of Oregon Medical School, 1940.

MORRISON, JONATHAN I., 19 Regent Circle, Brookline.
Dalhousie University Faculty of Medicine, 1940.

NEILL, MATHER H., 33 Francis Street, Needham.
Columbia University College of Physicians and Surgeons, 1943.

RIEMER, KARL, 552 Gay Street, Westwood.
Tufts College Medical School, 1940.

RISLEY, THOMAS S., 132 Gulliver Street, Milton.
Harvard Medical School, 1941.

ROWBOTHAM, JOHN L., 54 Pleasant Street, Canton.
Harvard Medical School, 1946.

SCOVILLE, PETER G., 15 Fairmount Avenue, Hyde Park.
College of Physicians and Surgeons, Boston, 1940. Sponsor: Henry Cabitt, 520 Beacon Street, Boston.

SEARS, ROBERT A., 164 Tappan Street, Brookline.
Yale University School of Medicine, 1943.

SHUMAN, SAMUEL B., 304 Washington Street, Dorchester.
Middlesex University School of Medicine, 1937. Sponsor: Irving J. Shalett, 1589 Beacon Street, Brookline.

SIEGEL, HENRY W., 46 Angell Street, Dorchester.
Middlesex University School of Medicine, 1942. Sponsor: Anthony West, 478 Gallivan Boulevard, Dorchester.

STANLEY, MALCOLM M., 37 Garrison Road, Brookline.
University of Louisville School of Medicine, 1941.

STONE, BARTLETT H., 394 Riverway, Brookline.
University of Vermont College of Medicine, 1941.

TANNENBAUM, HAROLD S., 339 Centre Street, Jamaica Plain.
Middlesex University School of Medicine, 1941. Sponsor: Bernard Lapidus, 16 Columbia Road, Dorchester.

WALLACE, ROBERT W., 1378 High Street, Westwood.
University of Pennsylvania School of Medicine, 1941.

WEISS, DANIEL M., 736 Morton Street, Dorchester.
Boston University School of Medicine, 1943.

WILKER, SYDNEY R., 97 Elm Hill Avenue, Roxbury.
Boston University School of Medicine, 1940.

Basil E. Barton, *Secretary*
10 Richwood Street, West Roxbury

NORFOLK SOUTH DISTRICT

CAREY, WILLIAM A., 28 Bridge Street, Quincy.
Yale University School of Medicine, 1941.

COOPER, MAURICE Z., 52 Florence Street, Wollaston.
Long Island College of Medicine, 1931.

HUNTER, HENRY J., 272 Pleasant Street, South Weymouth.
Temple University School of Medicine, 1940.

JACOBS, LEON G., 175 Franklin Street, Quincy.
Middlesex University School of Medicine, 1939. Sponsor: William S. Altman, 32 Spear Street, Quincy.

RUBIN, FRANK F., 795 Southern Artery, Quincy.
Middlesex University School of Medicine, 1937. Sponsor: Frederic N. Manley, 1200 Hancock Street, Quincy.

VAN KEUREN, HOWARD C., 34 Alden Road, Weymouth.
Albany Medical College, 1943.

Ebenezer K. Jenkins, *Secretary*
Norfolk County Hospital, South Braintree

PLYMOUTH DISTRICT

DEL COLLIANO, MICHAEL R., South Easton.
Middlesex University School of Medicine, 1936. Sponsor: George A. Moore, 167 Newbury Street, Brockton.

MAYO, WALTER V., 119 Summer Street, Kingston.
Middlesex University School of Medicine, 1936. Sponsor: Harold H. Hamilton, 70 Court Street, Plymouth.

PUTNAM, HAZEL E., 31 North Street, Plymouth.
McGill University Faculty of Medicine, 1944.

STEWART, GOODWILL M., 37 May Avenue, Brockton.
Tufts College Medical School, 1945.

THIERY, RAYMOND D., State Farm, Bridgewater.
Harvard Medical School, 1923.

Samuel Gale, *Secretary*
The Checkerton, Brockton

SUFFOLK DISTRICT

BILL, ALEXANDER H., JR., 522 Park Drive, Boston.
Harvard Medical School, 1939.

BRAZELTON, THOMAS B., 14 Pinckney Street, Boston.
Columbia University College of Physicians and Surgeons, 1943.

BRODERICK, THOMAS F., JR., 503 Beacon Street, Boston.
Tufts College Medical School, 1941.

CARTER, MAX G., 256 Beacon Street, Boston.
Harvard Medical School, 1941.

COMMONS, ROBERT R., Millwood Street, Framingham Centre.
Harvard Medical School, 1943.

DICKSON, WILLIAM A., 100 Rockwood Street, Jamaica Plain.
Cornell University Medical College, 1943.

GEPHART, FRANCIS T., 72 West Cedar Street, Boston.
Harvard Medical School, 1940.

HOFFMAN, SUMNER H., 102 Queensberry Street, Boston.
Tufts College Medical School, 1946.

KIEHL, KATHARINE, 6 Poplar Place, Boston.
University of Kansas School of Medicine, 1943.

LEARD, SAMUEL E., 86 East Newton Street, Boston.
Boston University School of Medicine, 1942.

McCARTER, ROBERT H., 74 Fenwood Road, Boston.
Jefferson Medical College of Philadelphia, 1942.

McDERMOTT, JOHN R., Boston City Hospital, Boston.
Yale University School of Medicine, 1941.

MAFFER, PETER A. R., 110 Barnes Avenue, East Boston.
Tufts College Medical School, 1942.

MARTIN, FRANCIS, Boston City Hospital, Boston.
Queen's University Faculty of Medicine, 1939.

MICHAELSON, ABRAHAM I., 97 Walnut Avenue, Revere.
Middlesex University School of Medicine, 1941. Sponsor: Louis Siegel, 72 Shirley Avenue, Revere.

NELSON, ROSEMARY, N. E. Hospital for Women and Children.
University of Chicago, The School of Medicine, 1939.

PROCTOR, WALLACE, 750 Harrison Avenue, Boston.
University of California Medical School, 1933.

ROBERTSON, CHARLES W., 152 Robbins Road, Watertown.
Syracuse University College of Medicine, 1939.

ROSS, HELEN M., 87 St. Stephen Street, Boston.
Tufts College Medical School, 1942.

VALENSTEIN, ARTHUR F., 107 Jersey Street, Boston.
Cornell University Medical College, 1938.

WELLER, THOMAS H., 8 Netherlands Road, Brookline.
Harvard Medical School, 1940.

Charles G. Shedd, *Secretary*
422 Beacon Street, Boston

WORCESTER DISTRICT

BACASTOW, MERLE S., Belmont Hospital, Worcester.
University of Pennsylvania School of Medicine, 1943.

BELL, HORACE S., 4 Creeper Hill Road, North Grafton.
Tufts College Medical School, 1943.

CLIFFORD, WILLIAM P. J., 51 Exchange Street, Milford.
Boston University School of Medicine, 1942.

DYKENS, JAMES W., 3 Gilman Street, Worcester.
University of Vermont College of Medicine, 1945.

GREEN, ROSS W., Memorial Hospital, Worcester.
Tufts College Medical School, 1943.

HARRIS, SIDNEY, 84 Commodore Road, Worcester.
New York University College of Medicine, 1934.

HURLEY, JOSEPH P., 26 Monroe Avenue, Worcester.
Tufts College Medical School, 1940.

Julius J. Tegelberg, *Secretary*
390 Main Street, Worcester

WORCESTER NORTH DISTRICT

ALEXANDER, DANIEL D., Gardner State Hospital, East Gardner.
Middlesex University School of Medicine, 1942. Sponsor: Charles E. Thompson, Gardner State Hospital, East Gardner.

COLLINGS, ROBERT Z., JR., Town Farm Road West, Westminster.
University of Chicago, The School of Medicine, 1939.

CRUDIM, MYRTLE B., Baldwinsville Hospital, Baldwinsville.
Marquette University School of Medicine, 1930.

GOLDMAN, SIDNEY, 79 Prichard Street, Fitchburg.
Middlesex University School of Medicine, 1941. Sponsor: John J. Curley, 82 Main Street, Leominster.

SIMON, AARON I., 41 Boutelle Street, Leominster.
Ohio State University College of Medicine, 1940.

James G. Simmons, *Secretary*
30 Myrtle Avenue, Fitchburg

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

TRANSFER OF MASSACHUSETTS BLOOD PROGRAM TO AMERICAN RED CROSS

Since the American National Red Cross has committed itself to providing free blood and blood products to all the people of this country, the Massachusetts Department of Public Health will relinquish its blood-program activities to the Red Cross as part of the established nationwide program.

Arrangements are already underway whereby the Red Cross will gradually assume the blood-program responsibilities now carried by the Massachusetts Department of Public Health. Thus, there will be no interruption in the operation of the program. The Red Cross will take over the project on or be-

fore June 30; therefore, no funds are being provided in the budget of the Department of Public Health after that date for the collection, processing or distribution of whole blood.

The transfer of the blood program from the Department of Public Health to the American National Red Cross has the approval of the Massachusetts Medical Society, as evidenced by the following motion passed at a recent meeting of the Council.

> . . . that the Council of the Massachusetts Medical Society approve in principle the transfer of the Program for the distribution of Whole Blood and Blood Fractions from the Massachusetts Department of Public Health to the American National Red Cross with the understanding that this Society and the Massachusetts Department of Public Health will serve in an advisory and consultative capacity to the American National Red Cross on this Program.

The statewide blood program in Massachusetts has entered its third year. A summary of the activities of the program shows that 318 visits have been made to communities throughout Massachusetts. Since many of the clinics ran for more than one day, the mobile units actually collected blood on four hundred and sixty-nine days.

As of January 31, 1948, blood donations to the program amounted to 30,796 pints. It is interesting that more than a third of this blood was collected during the past six months. Factors contributing to this increase in donations are the intensified publicity campaigns, the addition of a second mobile unit and especially the growing consciousness on the part of the general public of the value of such an organized program.

The blood program has already saved Massachusetts residents thousands of dollars annually by providing blood and blood products free of charge. During the last three months of 1947, an average of over 1600 pints of whole blood was distributed per month, saving patients over $40,000 a month for needed whole blood. In January, nearly 3000 units of gamma globulin, used for the modification of measles, was distributed to physicians in the Commonwealth. Commercially, this quantity of gamma globulin would have cost approximately $18,000. It is estimated that the blood and blood products now available or being processed for distribution are valued at nearly half a million dollars.

The Blood Processing Laboratory of the Massachusetts Department of Public Health will continue to function as a fractionation plant. Research will be carried on to improve and develop fractionation methods. Studies in progress have already revealed several interesting discoveries. It has been found that outdated plasma can be used in the preparation of acceptable albumin and gamma globulin. Both these fractions made from overage blood plasma have successfully passed laboratory tests, and albumin has already proved thoroughly satisfactory after trial injections into human beings.

More than 21,000 pints of blood was donated to the blood program last year. This amount of blood is only a small fraction of the whole-blood needs of the Commonwealth. To meet this great demand it is necessary for all residents in communities throughout Massachusetts to participate in and support the vital program that will be operated by the American National Red Cross.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Studies on the Influenza-A Epidemic of January–March 1941 at Groningen (Holland). By J. A. R. Van Bruggen, M.D., L. Bijlmer, M.D., W. A. Hoek, J. Mulder, M.D., and L. J. Zielstra. 8°, paper, 79 pp., with 26 illustrations. Verhandelingen Van Het Instituut Voor Preventieve Geneeskunde VII. Leiden: Stenfert Kroese, 1947. $2.00.

In this volume of proceedings the results of a study by a group of scientists on a short-term intensive epidemic of influenza A are recorded. There was a total of 117 cases, of which 44 were selected for research. Thirty-five of these cases were identified as influenza A virus infections by ferret inoculation and by mouse-protection and complement-fixation tests with patient serum. Three ferret strains were adapted to mice. These strains showed no differences in antigenic structure, but they were different from the WS strain. Clinically severe hyperemia with small vesicles of the anterior palatopharyngeal arches seemed to be a reliable diagnostic symptom in most cases. The authors believe that in cases of suspected influenza penicillin and the sulfonamides should be used as a prophylactic measure. During periods of malignant pandemic or interpandemic influenza large stocks of these remedies should be established in every country for the purpose of preventing pneumonia, especially staphylococcal pneumonia. The report discusses the epidemiology of the Groningen outbreak and presents a clinical survey of uncomplicated cases, bacterial complications of the respiratory tract, including acute tonsillitis in confirmed cases of influenza, virology and immunity reactions, the treatment and prophylaxis of bacterial lung complications. It concludes with a series of case reports, a summary and a list of references. The introduction discusses pandemic and interpandemic outbreaks and provides a list of all such epidemics in the world for the period 1933–1946. The illustrations are excellent. The lack of an index detracts from the usability of the work. The publishing is good. This monograph is recommended for all medical libraries.

Catalogue of the Mütter Museum of the College of Physicians of Philadelphia. Part I. Compiled by Ella N. Wade, Curator. 4°, paper, 89 pp. Philadelphia: College of Physicians, 1947.

In 1863 Dr. Thomas D. Mütter presented to the College of Physicians of Philadelphia his museum of normal and pathologic specimens. The collection was merged with one already in the possession of the College. The specimens today number over seventy-three hundred, and the only catalog available has been a typewritten copy in three volumes. In 1946 the idea of publishing a catalog was inaugurated and a general plan formulated, and after some regrouping of specimens this first part of the projected catalog was published in the *Transactions* of the College. Further installments will be published from time to time until the work is completed. The final installment will comprise a list of donors and an index. The College is congratulated upon making available a catalog of this fine collection.

Problems of Early Infancy. (Transactions of the First Conference March 3–4, 1947, New York City.) Edited by Milton J. E. Senn, Department of Pediatrics, Cornell University Medical College. 8°, paper, 70 pp. New York: Josiah Macy, Jr., Foundation, 1947. 75¢.

In this small volume the various papers read at the first conference on the problems of infancy are presented. Fourteen papers were read by psychiatrists, psychologists, social workers, pediatricians and obstetricians. The primary themes discussed were the importance of breast feeding and the rooming-in project, whereby the mother and newborn infant are kept together in one room, instead of being separated, and whereby the mother cares for her child so far as possible.

Specifische Typhustherapie mit einem Beitrag zur Typhuspathogenese. Von Dozent Dr. Ferdinand Nagl und Dr. Oskar Lachner. 8°, paper, 63 pp., with 32 illustrations. Wien: Verlag Wilhelm Maudrich, 1947.

This monograph discusses the vaccine treatment of typhoid fever and is based on the authors' experience in the Florisdorf Hospital in Vienna during 1945–1946. The total admissions were 359. Various methods of treatment were used for 272 cases, and vaccine therapy for 87 cases. The total mortality was 16.4 per cent (45 cases), but only 1 patient treated with vaccine died. The material is well organized and discusses allergy and immunity, pathogenesis, bacillemia, pathological anatomy, method of vaccine therapy, statistics and the clinical aspects, illustrated with a number of temperature charts. The paper, type and printing are excellent.

NOTICES

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, March 16, at 8:15 p.m. A symposium on thoracic surgery will be presented.

PROGRAM

Surgical Treatment of Carcinoma of the Esophagus. Dr. Richard H. Sweet.
Surgical Aspects of Pulmonary Disease. Dr. John W. Strieder.
A Survey of Current Heart Surgery. Dr. Dwight E. Harken.

NORFOLK DISTRICT MEDICAL SOCIETY

A meeting of the Norfolk District Medical Society will be held at the Boston Medical Library, 8 Fenway, Boston, on Tuesday, March 23, at 8 p.m.

A business meeting consisting of reading of minutes of the previous meeting, reports of committees, communications and new business will be held.

A scientific program entitled "Harvard Night" will be presented.

PROGRAM

Harvard Medical School: Present and future plans.
C. Sidney Burwell, M.D.
Acute Blood Dyscrasias.
Thomas H. Ham, M.D.
Replacement Therapy in Gastrointestinal Emergencies.
Chester M. Jones, M.D.
Certain Cardiac Emergencies.
Samuel A. Levine, M.D.
Surgical Treatment for Coarctation of the Aorta.
Robert E. Gross, M.D.

HARVARD SCHOOL OF PUBLIC HEALTH

The Harvard School of Public Health announces that the Cutter Lecture on Preventive Medicine, initiated in 1912, will be held in the amphitheater of Building D, Harvard Medical School, on Monday, April 12, at 5 p.m. Dr. William N. Pickles, medical officer of health, Aysgarth Rural District, Yorkshire, England, will speak on "Epidemiology in Country Practice."

The medical profession, medical and public-health students and others interested are cordially invited to attend.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY

The fourth annual national session of the American Society for the Study of Sterility will be held at the Congress Hotel, Chicago, on June 21 and 22. The two-day program will be divided into a special series of panel discussions on male infertility, with papers on female infertility and miscellaneous aspects on the second day.

The chairman is Professor Edwin G. Robertson, chairman, Department of Obstetrics and Gynecology, Queens University Faculty of Medicine, Ontario, Canada.

Additional information may be obtained from the secretary, Dr. John O. Haman, 490 Post Street, San Francisco 2, California.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MARCH 18

THURSDAY, MARCH 18
12:00 m. Medical Staff Meeting. Nurses Home, Allerton Hospital, Brookline.

FRIDAY, MARCH 19
*9:00–10:00 a.m. Some Aspects of Auscultation of the Heart. Dr. Samuel A. Levine. Joseph H. Pratt Diagnostic Hospital.
*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

MONDAY, MARCH 22
12:00 m. Clinicopathological Conference. Margaret Jewett Hall, Mt. Auburn Hospital, Cambridge.
*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

TUESDAY, MARCH 23
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
8:00 p.m. Norfolk District Medical Society. Boston Medical Library.

WEDNESDAY, MARCH 24
*9:00–10:00 a.m. The Etiology of Simple Goiter. Dr. Monte A. Greer. Joseph H. Pratt Diagnostic Hospital.
*12:00 m. Grand Rounds and Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

MARCH 12 and 13. American Association of Pathologists and Bacteriologists. Page 204, issue of February 5.

MARCH 16. Greater Boston Medical Society. Notice above.

MARCH 23. Norfolk District Medical Society. Notice above.

MARCH 28–APRIL 4. American Association of Industrial Physicians and Surgeons, American Industrial Hygiene Association, American Conference of Governmental Industrial Hygienists, American Association of Industrial Nurses, Inc., and American Association of Industrial Dentists. Hotel Statler, Boston.

APRIL 7, 9, 14 and 16. American Trudeau Society. Page 240, issue of February 12.

APRIL 8. Endometriosis. Dr. John Fallon. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

APRIL 10. American Congress of Physical Medicine. Page 344, issue of March 4.

APRIL 12. Harvard School of Public Health. Notice above.

APRIL 13. Harvard Medical Society, Amphitheater, Building D, Harvard Medical School.

APRIL 19–23. American College of Physicians. Page xiii, issue of July 31.

APRIL 29–MAY 2. American Academy of Pediatrics. Page 240, issue of February 12.

MAY 6. Suffolk Censors' Meeting. Page 344, issue of March 4.

MAY 6–8. American Association for the Study of Goiter. Page xiii, issue of July 31.

MAY 16–22. American Board of Obstetrics and Gynecology, Inc. Page 344, issue of March 4.

MAY 16–23. International College of Surgeons. Page 136, issue of January 22.

MAY 17–20. American Urological Association. Hotel Statler, Boston.

MAY 18–22. American Association on Mental Deficiency. Copley Plaza Hotel, Boston.

MAY 20–25. American Board of Ophthalmology. Page 170, issue of January 29.

(*Notices concluded on page xv*)